

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
8 April 2004 (08.04.2004)

PCT

(10) International Publication Number  
**WO 2004/028479 A2**

- (51) International Patent Classification<sup>7</sup>: **A61K** [US/US]; 41 Nevada Street, San Francisco, CA 94110 (US).
- (21) International Application Number: PCT/US2003/030907 (74) Agents: CARPENTER, David, A. et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).
- (22) International Filing Date: 25 September 2003 (25.09.2003) (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SI, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/414,006 25 September 2002 (25.09.2002) US
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- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— *without international search report and to be republished upon receipt of that report*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: NOUVELLES COMPOSITIONS ET METHODES DE TRAITEMENT DU PSORIASIS

(57) Abstract: La présente invention concerne des compositions contenant une nouvelle protéine ainsi que des méthodes d'utilisation desdites compositions pour le diagnostic et le traitement du psoriasis.

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WO 2004/028479 A2

## NOVEL COMPOSITIONS AND METHODS FOR THE TREATMENT OF PSORIASIS

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Field of the Invention

The present invention relates to compositions and methods useful for the diagnosis and treatment of psoriasis.

Background of the Invention

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Immune related and inflammatory diseases are the manifestation or consequence of fairly complex, often multiple interconnected biological pathways which in normal physiology are critical to respond to insult or injury, initiate repair from insult or injury, and mount innate and acquired defense against foreign organisms. Disease or pathology occurs when these normal physiological pathways cause additional insult or injury either as directly related to the intensity of the response, as a consequence of abnormal regulation or excessive stimulation, as a reaction to self, or as a combination of these.

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Though the genesis of these diseases often involves multistep pathways and often multiple different biological systems/pathways, intervention at critical points in one or more of these pathways can have an ameliorative or therapeutic effect. Therapeutic intervention can occur by either antagonism of a detrimental process/pathway or stimulation of a beneficial process/pathway.

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Many immune related diseases are known and have been extensively studied. Such diseases include immune-mediated inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency diseases, neoplasia, *etc.*

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T lymphocytes (T cells) are an important component of a mammalian immune response. T cells recognize antigens which are associated with a self-molecule encoded by genes within the major histocompatibility complex (MHC). The antigen may be displayed together with MHC molecules on the surface of antigen presenting cells, virus infected cells, cancer cells, grafts, *etc.* The T cell system eliminates these altered cells which pose a health threat to the host mammal. T cells include helper T cells and cytotoxic T cells. Helper T cells proliferate extensively following recognition of an antigen-MHC complex on an antigen presenting cell. Helper T cells also secrete a variety of cytokines, *i.e.*, lymphokines, which play a central role in the activation of B cells, cytotoxic T cells and a variety of other cells which participate in the immune response.

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Several diseases of the skin are correlated with an aberrant T cell response and to autoimmunity. Psoriasis is thought to be an autoimmune disease. Specifically, T-cells of the immune system recognize a protein in the skin and attack the area where that protein is found, causing the too-rapid growth of new skin cells and painful, elevated, scaly lesions. These lesions are characterized by hyperproliferation of keratinocytes and the accumulation of activated T-cells in the epidermis of the psoriatic lesions. There are several forms of psoriasis; guttate is the one that most commonly occurs in children and teens. It is sometimes preceded by an upper respiratory infection. Guttate psoriasis is noncontagious and characterized by small drop-like lesions, usually scattered over the trunk, limbs and scalp. According to the National Psoriasis Foundation, approximately seven million people in the United States have psoriasis. About 20,000

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children are diagnosed with psoriasis annually, and many of the cases are attributed to upper respiratory infections. It is estimated that only about 1.5 million people with psoriasis actually seek treatment, primarily due to lack of or dissatisfaction with current treatments. Although the initial molecular cause of disease is unknown, genetic linkages have been mapped to at least 7 psoriasis susceptibility loci (Psor1 on 6p21.3, Psor2 on 17q, Psor3 on 4q, Psor4 on 1 cent-q21, Psor5 on 3q21, Psor6 on 19p13, and Psor7 on 1p). Some of these loci overlap with other autoimmune/inflammatory diseases including rheumatoid arthritis, atopic dermatitis, and irritable bowel disease. In this application, experiments determine that a gene is upregulated in psoriatic skin vs. normal skin.

Despite the above identified advances in psoriasis research, there is a great need for additional diagnostic and therapeutic agents capable of detecting the presence of a psoriasis in a mammal and for effectively inhibiting this affliction. Accordingly, it is an objective of the present invention to identify polypeptides that are overexpressed in psoriasis as compared to normal skin, and to use those polypeptides, and their encoding nucleic acids, to produce compositions of matter useful in the therapeutic treatment and diagnostic detection of psoriasis in mammals.

#### Summary of the Invention

##### A. Embodiments

The present invention concerns compositions and methods useful for the diagnosis and treatment of psoriasis in mammals, including humans. The present invention is based on the identification of proteins (including agonist and antagonist antibodies) which are a result of psoriasis in mammals. Immune related diseases such as psoriasis may be treated by suppressing the immune response. Molecules that enhance the immune response stimulate or potentiate the immune response to an antigen. Molecules which stimulate the immune response can be used therapeutically where enhancement of the immune response would be beneficial. Alternatively, molecules that suppress the immune response attenuate or reduce the immune response to an antigen (e.g., neutralizing antibodies) can be used therapeutically where attenuation of the immune response would be beneficial (e.g., inflammation). Accordingly, the PRO polypeptides, agonists and antagonists thereof are also useful to prepare medicines and medicaments for the treatment of psoriasis. In a specific aspect, such medicines and medicaments comprise a therapeutically effective amount of a PRO polypeptide, agonist or antagonist thereof with a pharmaceutically acceptable carrier. Preferably, the admixture is sterile.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprises contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native sequence PRO polypeptide. In a specific aspect, the PRO agonist or antagonist is an anti-PRO antibody.

In another embodiment, the invention concerns a composition of matter comprising a PRO polypeptide or an agonist or antagonist antibody which binds the polypeptide in admixture with a carrier or excipient. In one aspect, the composition comprises a therapeutically effective amount of the polypeptide or antibody. In a further aspect, when the composition comprises a psoriasis inhibiting molecule, the composition is useful for: (a) reducing the amount of psoriasis tissue of a mammal in need thereof, (b)

inhibiting or reducing an auto-immune response in a mammal in need thereof. In another aspect, the composition comprises a further active ingredient, which may, for example, be a further antibody or a cytotoxic or chemotherapeutic agent. Preferably, the composition is sterile.

5 In another embodiment, the invention concerns a method of treating psoriasis in a mammal in need thereof, comprising administering to the mammal an effective amount of a PRO polypeptide, an agonist thereof, or an antagonist thereto.

10 In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody. In one aspect, the present invention concerns an isolated antibody which binds a PRO polypeptide. In another aspect, the antibody mimics the activity of a PRO polypeptide (an agonist antibody) or conversely the antibody inhibits or neutralizes the activity of a PRO polypeptide (an antagonist antibody). In another aspect, the antibody is a monoclonal antibody, which preferably has nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues. The antibody may be labeled and may be immobilized on a solid support. In a further aspect, 15 the antibody is an antibody fragment, a monoclonal antibody, a single-chain antibody, or an anti-idiotypic antibody.

In yet another embodiment, the present invention provides a composition comprising an anti-PRO antibody in admixture with a pharmaceutically acceptable carrier. In one aspect, the composition comprises a therapeutically effective amount of the antibody. Preferably, the composition is sterile. The composition 20 may be administered in the form of a liquid pharmaceutical formulation, which may be preserved to achieve extended storage stability. Alternatively, the antibody is a monoclonal antibody, an antibody fragment, a humanized antibody, or a single-chain antibody.

In a further embodiment, the invention concerns an article of manufacture, comprising:

- 25 (a) a composition of matter comprising a PRO polypeptide or agonist or antagonist thereof;  
(b) a container containing said composition; and  
(c) a label affixed to said container, or a package insert included in said container referring to the use of said PRO polypeptide or agonist or antagonist thereof in the treatment of an immune related disease. The composition may comprise a therapeutically effective amount of the PRO polypeptide or the agonist or antagonist thereof.

30 In yet another embodiment, the present invention concerns a method of diagnosing psoriasis in a mammal, comprising detecting the level of expression of a gene encoding a PRO polypeptide (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower expression level in the test sample as compared to the control sample indicates the presence of psoriasis in the mammal from which the test tissue cells were 35 obtained.

In another embodiment, the present invention concerns a method of diagnosing psoriasis in a mammal, comprising (a) contacting an anti-PRO antibody with a test sample of tissue cells obtained from the mammal, and (b) detecting the formation of a complex between the antibody and a PRO polypeptide, in the test sample; wherein the formation of said complex is indicative of the presence or absence of said 40 psoriasis. The detection may be qualitative or quantitative, and may be performed in comparison with



monitoring the complex formation in a control sample of known normal tissue cells of the same cell type. A larger quantity of complexes formed in the test sample indicates the presence or absence of psoriasis in the mammal from which the test tissue cells were obtained. The antibody preferably carries a detectable label. Complex formation can be monitored, for example, by light microscopy, flow cytometry, fluorimetry, or other techniques known in the art. The test sample is usually obtained from an individual suspected of having psoriasis.

In another embodiment, the invention provides a method for determining the presence of a PRO polypeptide in a sample comprising exposing a test sample of cells suspected of containing the PRO polypeptide to an anti-PRO antibody and determining the binding of said antibody to said cell sample. In a specific aspect, the sample comprises a cell suspected of containing the PRO polypeptide and the antibody binds to the cell. The antibody is preferably detectably labeled and/or bound to a solid support.

In another embodiment, the present invention concerns a psoriasis diagnostic kit, comprising an anti-PRO antibody and a carrier in suitable packaging. The kit preferably contains instructions for using the antibody to detect the presence of the PRO polypeptide. Preferably the carrier is pharmaceutically acceptable.

In another embodiment, the present invention concerns a diagnostic kit, containing an anti-PRO antibody in suitable packaging. The kit preferably contains instructions for using the antibody to detect the PRO polypeptide.

In another embodiment, the invention provides a method of diagnosing an psoriasis in a mammal which comprises detecting the presence or absence of a PRO polypeptide in a test sample of tissue cells obtained from said mammal, wherein the presence or absence of the PRO polypeptide in said test sample is indicative of the presence of psoriasis in said mammal.

In another embodiment, the present invention concerns a method for identifying an agonist of a PRO polypeptide comprising:

- (a) contacting cells and a test compound to be screened under conditions suitable for the induction of a cellular response normally induced by a PRO polypeptide; and
- (b) determining the induction of said cellular response to determine if the test compound is an effective agonist, wherein the induction of said cellular response is indicative of said test compound being an effective agonist.

In another embodiment, the invention concerns a method for identifying a compound capable of inhibiting the activity of a PRO polypeptide comprising contacting a candidate compound with a PRO polypeptide under conditions and for a time sufficient to allow these two components to interact and determining whether the activity of the PRO polypeptide is inhibited. In a specific aspect, either the candidate compound or the PRO polypeptide is immobilized on a solid support. In another aspect, the non-immobilized component carries a detectable label. In a preferred aspect, this method comprises the steps of:

- (a) contacting cells and a test compound to be screened in the presence of a PRO polypeptide under conditions suitable for the induction of a cellular response normally induced by a PRO polypeptide; and
- (b) determining the induction of said cellular response to determine if the test compound is an effective antagonist.

In another embodiment, the invention provides a method for identifying a compound that inhibits

the expression of a PRO polypeptide in cells that normally express the polypeptide, wherein the method comprises contacting the cells with a test compound and determining whether the expression of the PRO polypeptide is inhibited. In a preferred aspect, this method comprises the steps of:

- (a) contacting cells and a test compound to be screened under conditions suitable for allowing  
5 expression of the PRO polypeptide; and
- (b) determining the inhibition of expression of said polypeptide.

In yet another embodiment, the present invention concerns a method for treating psoriasis in a mammal that suffers therefrom comprising administering to the mammal a nucleic acid molecule that codes for either (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide or (c) an antagonist of a PRO  
10 polypeptide, wherein said agonist or antagonist may be an anti-PRO antibody. In a preferred embodiment, the mammal is human. In another preferred embodiment, the nucleic acid is administered via *ex vivo* gene therapy. In a further preferred embodiment, the nucleic acid is comprised within a vector, more preferably an adenoviral, adeno-associated viral, lentiviral or retroviral vector.

In yet another aspect, the invention provides a recombinant viral particle comprising a viral vector  
15 consisting essentially of a promoter, nucleic acid encoding (a) a PRO polypeptide, (b) an agonist polypeptide of a PRO polypeptide, or (c) an antagonist polypeptide of a PRO polypeptide, and a signal sequence for cellular secretion of the polypeptide, wherein the viral vector is in association with viral structural proteins. Preferably, the signal sequence is from a mammal, such as from a native PRO polypeptide.

In a still further embodiment, the invention concerns an *ex vivo* producer cell comprising a nucleic  
20 acid construct that expresses retroviral structural proteins and also comprises a retroviral vector consisting essentially of a promoter, nucleic acid encoding (a) a PRO polypeptide, (b) an agonist polypeptide of a PRO polypeptide or (c) an antagonist polypeptide of a PRO polypeptide, and a signal sequence for cellular secretion of the polypeptide, wherein said producer cell packages the retroviral vector in association with the structural proteins to produce recombinant retroviral particles.

#### 25 B. Additional Embodiments

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions  
30 suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeptides fused to a heterologous polypeptide or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeptides fused to an epitope tag sequence or a  
35 Fc region of an immunoglobulin.

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody.

In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences or as antisense probes, wherein those probes may be derived from any of the above or below described nucleotide sequences.

In other embodiments, the invention provides an isolated nucleic acid molecule comprising a  
5 nucleotide sequence that encodes a PRO polypeptide.

In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about  
10 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid  
15 sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule encoding a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid  
20 sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid  
25 sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about  
30 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid  
35 sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide lacking the signal peptide as disclosed herein, the coding sequence of an extracellular domain of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein or the coding sequence of any other specifically defined fragment of the full-length amino acid  
40 sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs as disclosed herein, or (b) the complement of the DNA molecule of (a).

Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Another embodiment is directed to fragments of a PRO polypeptide coding sequence, or the complement thereof, that may find use as, for example, hybridization probes, for encoding fragments of a PRO polypeptide that may optionally encode a polypeptide comprising a binding site for an anti-PRO antibody or as antisense oligonucleotide probes. Such nucleic acid fragments are usually at least about 20 nucleotides in length, alternatively at least about 30 nucleotides in length, alternatively at least about 40 nucleotides in length, alternatively at least about 50 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 70 nucleotides in length, alternatively at least about 80 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 110 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 130 nucleotides in length, alternatively at least about 140 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 160 nucleotides in length, alternatively at least about 170 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 190 nucleotides in length, alternatively at least about 200 nucleotides in length, alternatively at least about 250 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 350 nucleotides in length, alternatively at least about 400 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 500 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 700 nucleotides in length, alternatively at least about 800 nucleotides in length, alternatively at least about 900 nucleotides in length and alternatively at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length.

It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences herein above identified.

In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an amino acid sequence encoded by any of the human protein cDNAs as disclosed herein.

In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as herein before described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined herein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody or a small molecule.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist or antagonist thereof as herein before described, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The Figures 1-2484 show the nucleic acids of the invention and their encoded PRO polypeptides.

Figure 1 shows a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO83270 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "DNA326953".

Figure 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in Figure 1.

Figure 3 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO60747 cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA272614".

Figure 4 shows the amino acid sequence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in Figure 3.

Figure 5 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO2690 cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA88189".

Figure 6 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in Figure 5.

Figure 7 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO61604 cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA272992".

5 Figure 8 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in Figure 7.

Figure 9A-B shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO83571 cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA327520".

10 Figure 10 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in Figure 9A-B.

Figure 11 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO58320 cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA327521".

Figure 12 shows the amino acid sequence (SEQ ID NO:12) derived from the coding sequence of SEQ ID NO:11 shown in Figure 11.

15 Figure 13 shows a nucleotide sequence (SEQ ID NO:13) of a native sequence PRO2874 cDNA, wherein SEQ ID NO:13 is a clone designated herein as "DNA327522".

Figure 14 shows the amino acid sequence (SEQ ID NO:14) derived from the coding sequence of SEQ ID NO:13 shown in Figure 13.

20 Figure 15A-B shows a nucleotide sequence (SEQ ID NO:15) of a native sequence PRO49240 cDNA, wherein SEQ ID NO:15 is a clone designated herein as "DNA254177".

Figure 16 shows the amino acid sequence (SEQ ID NO:16) derived from the coding sequence of SEQ ID NO:15 shown in Figure 15A-B.

Figure 17 shows a nucleotide sequence (SEQ ID NO:17) of a native sequence PRO59307 cDNA, wherein SEQ ID NO:17 is a clone designated herein as "DNA270977".

25 Figure 18 shows the amino acid sequence (SEQ ID NO:18) derived from the coding sequence of SEQ ID NO:17 shown in Figure 17.

Figure 19 shows a nucleotide sequence (SEQ ID NO:19) of a native sequence PRO4619 cDNA, wherein SEQ ID NO:19 is a clone designated herein as "DNA103298".

30 Figure 20 shows the amino acid sequence (SEQ ID NO:20) derived from the coding sequence of SEQ ID NO:19 shown in Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO38028 cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA327523".

Figure 22 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in Figure 21.

35 Figure 23A-B shows a nucleotide sequence (SEQ ID NO:23) of a native sequence PRO83572 cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA327524".

Figure 24 shows the amino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in Figure 23A-B.

40 Figure 25 shows a nucleotide sequence (SEQ ID NO:25) of a native sequence PRO2065 cDNA, wherein SEQ ID NO:25 is a clone designated herein as "DNA326839".

Figure 26 shows the amino acid sequence (SEQ ID NO:26) derived from the coding sequence of SEQ ID NO:25 shown in Figure 25.

Figure 27A-C shows a nucleotide sequence (SEQ ID NO:27) of a native sequence PRO83573 cDNA, wherein SEQ ID NO:27 is a clone designated herein as "DNA327525".

5        Figure 28 shows the amino acid sequence (SEQ ID NO:28) derived from the coding sequence of SEQ ID NO:27 shown in Figure 27A-C.

Figure 29 shows a nucleotide sequence (SEQ ID NO:29) of a native sequence PRO83574 cDNA, wherein SEQ ID NO:29 is a clone designated herein as "DNA327526".

10       Figure 30 shows the amino acid sequence (SEQ ID NO:30) derived from the coding sequence of SEQ ID NO:29 shown in Figure 29.

Figure 31 shows a nucleotide sequence (SEQ ID NO:31) of a native sequence PRO83575 cDNA, wherein SEQ ID NO:31 is a clone designated herein as "DNA327527".

Figure 32 shows the amino acid sequence (SEQ ID NO:32) derived from the coding sequence of SEQ ID NO:31 shown in Figure 31.

15       Figure 33A-B shows a nucleotide sequence (SEQ ID NO:33) of a native sequence PRO83576 cDNA, wherein SEQ ID NO:33 is a clone designated herein as "DNA327528".

Figure 34 shows the amino acid sequence (SEQ ID NO:34) derived from the coding sequence of SEQ ID NO:33 shown in Figure 33A-B.

20       Figure 35 shows a nucleotide sequence (SEQ ID NO:35) of a native sequence PRO83577 cDNA, wherein SEQ ID NO:35 is a clone designated herein as "DNA327529".

Figure 36 shows the amino acid sequence (SEQ ID NO:36) derived from the coding sequence of ~~SEQ ID NO:35 shown in Figure 35.~~

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Figure 37 shows a nucleotide sequence (SEQ ID NO:37) of a native sequence PRO83578 cDNA, wherein SEQ ID NO:37 is a clone designated herein as "DNA327530".

25       Figure 38 shows the amino acid sequence (SEQ ID NO:38) derived from the coding sequence of SEQ ID NO:37 shown in Figure 37.

Figure 39 shows a nucleotide sequence (SEQ ID NO:39) of a native sequence PRO12077 cDNA, wherein SEQ ID NO:39 is a clone designated herein as "DNA324468".

30       Figure 40 shows the amino acid sequence (SEQ ID NO:40) derived from the coding sequence of SEQ ID NO:39 shown in Figure 39.

Figure 41 shows a nucleotide sequence (SEQ ID NO:41) of a native sequence PRO83579 cDNA, wherein SEQ ID NO:41 is a clone designated herein as "DNA327531".

Figure 42 shows the amino acid sequence (SEQ ID NO:42) derived from the coding sequence of SEQ ID NO:41 shown in Figure 41.

35       Figure 42 shows a nucleotide sequence (SEQ ID NO:42) of a native sequence PRO71901 cDNA, wherein SEQ ID NO:42 is a clone designated herein as "DNA325124".

Figure 43 shows the amino acid sequence (SEQ ID NO:43) derived from the coding sequence of SEQ ID NO:44 shown in Figure 44.

40       Figure 45 shows a nucleotide sequence (SEQ ID NO:45) of a native sequence PRO71134 cDNA, wherein SEQ ID NO:45 is a clone designated herein as "DNA327532".



Figure 46 shows the amino acid sequence (SEQ ID NO:46) derived from the coding sequence of SEQ ID NO:45 shown in Figure 45.

Figure 47 shows a nucleotide sequence (SEQ ID NO:47) of a native sequence PRO36526 cDNA, wherein SEQ ID NO:47 is a clone designated herein as "DNA327533".

5        Figure 48 shows the amino acid sequence (SEQ ID NO:48) derived from the coding sequence of SEQ ID NO:47 shown in Figure 47.

Figure 49 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO62529 cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA274759".

10       Figure 50 shows the amino acid sequence (SEQ ID NO:50) derived from the coding sequence of SEQ ID NO:49 shown in Figure .

Figure 51 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO62782 cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA275062".

Figure 52 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ ID NO:51 shown in Figure 51.

15       Figure 53 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO2758 cDNA, wherein SEQ ID NO:58 is a clone designated herein as "DNA88350".

Figure 54 shows the amino acid sequence (SEQ ID NO:54) derived from the coding sequence of SEQ ID NO:53 shown in Figure 53.

20       Figure 55A-B shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO41180 cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA327534".

Figure 56 shows the amino acid sequence (SEQ ID NO:56) derived from the coding sequence of ~~SEQ ID NO:55 shown in Figure 55A-B .~~

Figure 57 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO39268 cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA287207".

25       Figure 58 shows the amino acid sequence (SEQ ID NO:58) derived from the coding sequence of SEQ ID NO:57 shown in Figure 57.

Figure 59 shows a nucleotide sequence (SEQ ID NO:59) of a native sequence PRO83580 cDNA, wherein SEQ ID NO:59 is a clone designated herein as "DNA327535".

30       Figure 60 shows the amino acid sequence (SEQ ID NO:60) derived from the coding sequence of SEQ ID NO:59 shown in Figure 59.

Figure 61 shows a nucleotide sequence (SEQ ID NO:61) of a native sequence PRO59895 cDNA, wherein SEQ ID NO:61 is a clone designated herein as "DNA271608".

Figure 62 shows the amino acid sequence (SEQ ID NO:62) derived from the coding sequence of SEQ ID NO:61 shown in Figure 61.

35       Figure 63A-B shows a nucleotide sequence (SEQ ID NO:63) of a native sequence PRO37003 cDNA, wherein SEQ ID NO:63 is a clone designated herein as "DNA327536".

Figure 64 shows the amino acid sequence (SEQ ID NO:64) derived from the coding sequence of SEQ ID NO:63 shown in Figure 63A-B.

40       Figure 65 shows a nucleotide sequence (SEQ ID NO:65) of a native sequence PRO3344 cDNA, wherein SEQ ID NO:65 is a clone designated herein as "DNA196817".

Figure 66 shows the amino acid sequence (SEQ ID NO:66) derived from the coding sequence of SEQ ID NO:65 shown in Figure 65.

Figure 67A-B shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO83581 cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA327537".

5        Figure 68 shows the amino acid sequence (SEQ ID NO:68) derived from the coding sequence of SEQ ID NO:67 shown in Figure 67A-B.

Figure 69 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO10315 cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA327538".

10       Figure 70 shows the amino acid sequence (SEQ ID NO:70) derived from the coding sequence of SEQ ID NO:69 shown in Figure 69.

Figure 71A-B shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO12211 cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA327539".

Figure 72 shows the amino acid sequence (SEQ ID NO:72) derived from the coding sequence of SEQ ID NO:71 shown in Figure 71A-B.

15       Figure 73 shows a nucleotide sequence (SEQ ID NO:73) of a native sequence PRO36587 cDNA, wherein SEQ ID NO:73 is a clone designated herein as "DNA226124".

Figure 74 shows the amino acid sequence (SEQ ID NO:74) derived from the coding sequence of SEQ ID NO:73 shown in Figure 73.

20       Figure 75 shows a nucleotide sequence (SEQ ID NO:75) of a native sequence PRO37082 cDNA, wherein SEQ ID NO:75 is a clone designated herein as "DNA226619".

Figure 76 shows the amino acid sequence (SEQ ID NO:76) derived from the coding sequence of ~~SEQ ID NO:75 shown in Figure 75.~~

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Figure 77 shows a nucleotide sequence (SEQ ID NO:77) of a native sequence PRO37540 cDNA, wherein SEQ ID NO:77 is a clone designated herein as "DNA227077".

25       Figure 78 shows the amino acid sequence (SEQ ID NO:78) derived from the coding sequence of SEQ ID NO:77 shown in Figure 77.

Figure 79 shows a nucleotide sequence (SEQ ID NO:79) of a native sequence PRO38005 cDNA, wherein SEQ ID NO:79 is a clone designated herein as "DNA327540".

30       Figure 80 shows the amino acid sequence (SEQ ID NO:80) derived from the coding sequence of SEQ ID NO:79 shown in Figure 79.

Figure 81 shows a nucleotide sequence (SEQ ID NO:81) of a native sequence PRO36341 cDNA, wherein SEQ ID NO:81 is a clone designated herein as "DNA225878".

Figure 80 shows the amino acid sequence (SEQ ID NO:80) derived from the coding sequence of SEQ ID NO:81 shown in Figure 81.

35       Figure 83 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO60864 cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA272753".

Figure 84 shows the amino acid sequence (SEQ ID NO:84) derived from the coding sequence of SEQ ID NO:83 shown in Figure 83.

40       Figure 85 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO71139 cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA304713".

Figure 86 shows the amino acid sequence (SEQ ID NO:86) derived from the coding sequence of SEQ ID NO:85 shown in Figure 85.

Figure 87 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO60225 cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA298609".

5        Figure 88 shows the amino acid sequence (SEQ ID NO:88) derived from the coding sequence of SEQ ID NO:87 shown in Figure 87.

Figure 89 shows a nucleotide sequence (SEQ ID NO:89) of a native sequence PRO71267 cDNA, wherein SEQ ID NO:89 is a clone designated herein as "DNA304872".

10       Figure 90 shows the amino acid sequence (SEQ ID NO:90) derived from the coding sequence of SEQ ID NO:89 shown in Figure 89.

Figure 91 shows a nucleotide sequence (SEQ ID NO:91) of a native sequence PRO82678 cDNA, wherein SEQ ID NO:91 is a clone designated herein as "DNA326273".

Figure 92 shows the amino acid sequence (SEQ ID NO:92) derived from the coding sequence of SEQ ID NO:91 shown in Figure 91.

15       Figure 93A-B shows a nucleotide sequence (SEQ ID NO:93) of a native sequence PRO2672 cDNA, wherein SEQ ID NO:93 is a clone designated herein as "DNA326191".

Figure 94 shows the amino acid sequence (SEQ ID NO:94) derived from the coding sequence of SEQ ID NO:93 shown in Figure 93.

20       Figure 95A-B shows a nucleotide sequence (SEQ ID NO:95) of a native sequence PRO2621 cDNA, wherein SEQ ID NO:95 is a clone designated herein as "DNA327541".

Figure 96 shows the amino acid sequence (SEQ ID NO:96) derived from the coding sequence of ~~SEQ ID NO:96 shown in Figure 95A-B.~~

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Figure 97 shows a nucleotide sequence (SEQ ID NO:97) of a native sequence PRO12890 cDNA, wherein SEQ ID NO:97 is a clone designated herein as "DNA151802".

25       Figure 98 shows the amino acid sequence (SEQ ID NO:98) derived from the coding sequence of SEQ ID NO:97 shown in Figure 97.

Figure 99 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO60221 cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA271945".

30       Figure 100 shows the amino acid sequence (SEQ ID NO:100) derived from the coding sequence of SEQ ID NO:99 shown in Figure 99.

Figure 101 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO39294 cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA239053".

Figure 102 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ ID NO:101 shown in Figure 101.

35       Figure 103 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO83582 cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA327542".

Figure 104 shows the amino acid sequence (SEQ ID NO:104) derived from the coding sequence of SEQ ID NO:103 shown in Figure 103.

40       Figure 105 shows a nucleotide sequence (SEQ ID NO:105) of a native sequence PRO80554 cDNA, wherein SEQ ID NO:105 is a clone designated herein as "DNA323805".

Figure 106 shows the amino acid sequence (SEQ ID NO:106) derived from the coding sequence of SEQ ID NO:105 shown in Figure 105.

Figure 107 shows a nucleotide sequence (SEQ ID NO:107) of a native sequence PRO62241 cDNA, wherein SEQ ID NO:107 is a clone designated herein as "DNA327543".

5        Figure 108 shows the amino acid sequence (SEQ ID NO:108) derived from the coding sequence of SEQ ID NO:107 shown in Figure 107.

Figure 109 shows a nucleotide sequence (SEQ ID NO:109) of a native sequence PRO70357 cDNA, wherein SEQ ID NO:109 is a clone designated herein as "DNA327544".

10       Figure 108 shows the amino acid sequence (SEQ ID NO:108) derived from the coding sequence of SEQ ID NO:109 shown in Figure 109.

Figure 111A-B shows a nucleotide sequence (SEQ ID NO:111) of a native sequence PRO82731 cDNA, wherein SEQ ID NO:111 is a clone designated herein as "DNA327545".

Figure 112 shows the amino acid sequence (SEQ ID NO:112) derived from the coding sequence of SEQ ID NO:111 shown in Figure 111A-B.

15       Figure 113 shows a nucleotide sequence (SEQ ID NO:113) of a native sequence cDNA, wherein SEQ ID NO:113 is a clone designated herein as "DNA327546".

Figure 114 shows a nucleotide sequence (SEQ ID NO:114) of a native sequence PRO83583 cDNA, wherein SEQ ID NO:114 is a clone designated herein as "DNA327547".

20       Figure 115 shows the amino acid sequence (SEQ ID NO:115) derived from the coding sequence of SEQ ID NO:114 shown in Figure 114.

Figure 116 shows a nucleotide sequence (SEQ ID NO:116) of a native sequence PRO12618 cDNA, wherein SEQ ID NO:116 is a clone designated herein as "DNA151148".

Figure 117 shows the amino acid sequence (SEQ ID NO:117) derived from the coding sequence of SEQ ID NO:116 shown in Figure 116.

25       Figure 118 shows a nucleotide sequence (SEQ ID NO:118) of a native sequence PRO81281 cDNA, wherein SEQ ID NO:118 is a clone designated herein as "DNA327548".

Figure 119 shows the amino acid sequence (SEQ ID NO:119) derived from the coding sequence of SEQ ID NO:118 shown in Figure 118.

30       Figure 120A-B shows a nucleotide sequence (SEQ ID NO:120) of a native sequence PRO83584 cDNA, wherein SEQ ID NO:120 is a clone designated herein as "DNA327549".

Figure 121 shows the amino acid sequence (SEQ ID NO:121) derived from the coding sequence of SEQ ID NO:120 shown in Figure 120A-B.

Figure 122 shows a nucleotide sequence (SEQ ID NO:122) of a native sequence PRO81164 cDNA, wherein SEQ ID NO:122 is a clone designated herein as "DNA327550".

35       Figure 123 shows the amino acid sequence (SEQ ID NO:123) derived from the coding sequence of SEQ ID NO:122 shown in Figure 122.

Figure 124A-B shows a nucleotide sequence (SEQ ID NO:124) of a native sequence PRO4797 cDNA, wherein SEQ ID NO:124 is a clone designated herein as "DNA103470".

40       Figure 125 shows the amino acid sequence (SEQ ID NO:125) derived from the coding sequence of SEQ ID NO:124 shown in Figure 124.

Figure 126 shows a nucleotide sequence (SEQ ID NO:126) of a native sequence PRO4650 cDNA, wherein SEQ ID NO:126 is a clone designated herein as "DNA103320".

Figure 127 shows the amino acid sequence (SEQ ID NO:127) derived from the coding sequence of SEQ ID NO:126 shown in Figure 126.

5        Figure 128 shows a nucleotide sequence (SEQ ID NO:128) of a native sequence PRO59289 cDNA, wherein SEQ ID NO:128 is a clone designated herein as "DNA327551".

Figure 129 shows the amino acid sequence (SEQ ID NO:129) derived from the coding sequence of SEQ ID NO:128 shown in Figure 128.

10       Figure 130 shows a nucleotide sequence (SEQ ID NO:130) of a native sequence PRO22664 cDNA, wherein SEQ ID NO:130 is a clone designated herein as "DNA327552".

Figure 131 shows the amino acid sequence (SEQ ID NO:131) derived from the coding sequence of SEQ ID NO:130 shown in Figure 130.

Figure 132 shows a nucleotide sequence (SEQ ID NO:132) of a native sequence PRO2679 cDNA, wherein SEQ ID NO:132 is a clone designated herein as "DNA88166".

15       Figure 133 shows the amino acid sequence (SEQ ID NO:133) derived from the coding sequence of SEQ ID NO:132 shown in Figure 132.

Figure 134 shows a nucleotide sequence (SEQ ID NO:134) of a native sequence PRO37073 cDNA, wherein SEQ ID NO:134 is a clone designated herein as "DNA304459".

20       Figure 135 shows the amino acid sequence (SEQ ID NO:135) derived from the coding sequence of SEQ ID NO:134 shown in Figure 134.

Figure 136 shows a nucleotide sequence (SEQ ID NO:136) of a native sequence PRO37073 cDNA, wherein SEQ ID NO:136 is a clone designated herein as "DNA304459".

Figure 137 shows the amino acid sequence (SEQ ID NO:137) derived from the coding sequence of SEQ ID NO:136 shown in Figure 136.

25       Figure 138A-B shows a nucleotide sequence (SEQ ID NO:138) of a native sequence PRO83585 cDNA, wherein SEQ ID NO:138 is a clone designated herein as "DNA327553".

Figure 139 shows the amino acid sequence (SEQ ID NO:139) derived from the coding sequence of SEQ ID NO:138 shown in Figure 138A-B.

30       Figure 140 shows a nucleotide sequence (SEQ ID NO:140) of a native sequence PRO59386 cDNA, wherein SEQ ID NO:140 is a clone designated herein as "DNA327554".

Figure 141 shows the amino acid sequence (SEQ ID NO:141) derived from the coding sequence of SEQ ID NO:140 shown in Figure 140.

Figure 142 shows a nucleotide sequence (SEQ ID NO:142) of a native sequence PRO83586 cDNA, wherein SEQ ID NO:142 is a clone designated herein as "DNA327555".

35       Figure 143 shows the amino acid sequence (SEQ ID NO:143) derived from the coding sequence of SEQ ID NO:142 shown in Figure 142.

Figure 144 shows a nucleotide sequence (SEQ ID NO:144) of a native sequence PRO2551 cDNA, wherein SEQ ID NO:144 is a clone designated herein as "DNA79129".

40       Figure 145 shows the amino acid sequence (SEQ ID NO:145) derived from the coding sequence of SEQ ID NO:144 shown in Figure 144.

Figure 146 shows a nucleotide sequence (SEQ ID NO:146) of a native sequence PRO83587 cDNA, wherein SEQ ID NO:146 is a clone designated herein as "DNA327556".

Figure 147 shows the amino acid sequence (SEQ ID NO:147) derived from the coding sequence of SEQ ID NO:146 shown in Figure 146.

5        Figure 148 shows a nucleotide sequence (SEQ ID NO:148) of a native sequence PRO2804 cDNA, wherein SEQ ID NO:148 is a clone designated herein as "DNA88464".

Figure 149 shows the amino acid sequence (SEQ ID NO:149) derived from the coding sequence of SEQ ID NO:148 shown in Figure 148.

10       Figure 150 shows a nucleotide sequence (SEQ ID NO:150) of a native sequence PRO62244 cDNA, wherein SEQ ID NO:150 is a clone designated herein as "DNA274326".

Figure 151 shows the amino acid sequence (SEQ ID NO:151) derived from the coding sequence of SEQ ID NO:150 shown in Figure 150.

Figure 152A-B shows a nucleotide sequence (SEQ ID NO:152) of a native sequence PRO37659 cDNA, wherein SEQ ID NO:152 is a clone designated herein as "DNA227196".

15       Figure 153 shows the amino acid sequence (SEQ ID NO:153) derived from the coding sequence of SEQ ID NO:152 shown in Figure 152A-B.

Figure 154 shows a nucleotide sequence (SEQ ID NO:154) of a native sequence PRO50473 cDNA, wherein SEQ ID NO:154 is a clone designated herein as "DNA255406".

20       Figure 155 shows the amino acid sequence (SEQ ID NO:155) derived from the coding sequence of SEQ ID NO:154 shown in Figure 154.

Figure 156 shows a nucleotide sequence (SEQ ID NO:156) of a native sequence PRO83588 cDNA, wherein SEQ ID NO:156 is a clone designated herein as "DNA327557".

Figure 157 shows the amino acid sequence (SEQ ID NO:157) derived from the coding sequence of SEQ ID NO:156 shown in Figure 156.

25       Figure 158A-B shows a nucleotide sequence (SEQ ID NO:158) of a native sequence PRO12515 cDNA, wherein SEQ ID NO:158 is a clone designated herein as "DNA327558".

Figure 159 shows the amino acid sequence (SEQ ID NO:159) derived from the coding sequence of SEQ ID NO:158 shown in Figure 158A-B.

30       Figure 160 shows a nucleotide sequence (SEQ ID NO:160) of a native sequence PRO70353 cDNA, wherein SEQ ID NO:160 is a clone designated herein as "DNA290244".

Figure 161 shows the amino acid sequence (SEQ ID NO:161) derived from the coding sequence of SEQ ID NO:160 shown in Figure 160.

Figure 162 shows a nucleotide sequence (SEQ ID NO:162) of a native sequence PRO70329 cDNA, wherein SEQ ID NO:162 is a clone designated herein as "DNA290232".

35       Figure 163 shows the amino acid sequence (SEQ ID NO:163) derived from the coding sequence of SEQ ID NO:162 shown in Figure 162.

Figure 164A-B shows a nucleotide sequence (SEQ ID NO:164) of a native sequence PRO12561 cDNA, wherein SEQ ID NO:164 is a clone designated herein as "DNA150966".

40       Figure 165 shows the amino acid sequence (SEQ ID NO:165) derived from the coding sequence of SEQ ID NO:164 shown in Figure 164A-B.

Figure 166 shows a nucleotide sequence (SEQ ID NO:166) of a native sequence PRO38039 cDNA, wherein SEQ ID NO:166 is a clone designated herein as "DNA227576".

Figure 167 shows the amino acid sequence (SEQ ID NO:167) derived from the coding sequence of SEQ ID NO:166 shown in Figure 166.

5        Figure 168 shows a nucleotide sequence (SEQ ID NO:168) of a native sequence PRO12769 cDNA, wherein SEQ ID NO:168 is a clone designated herein as "DNA150429".

Figure 169 shows the amino acid sequence (SEQ ID NO:169) derived from the coding sequence of SEQ ID NO:168 shown in Figure 168.

10       Figure 170 shows a nucleotide sequence (SEQ ID NO:170) of a native sequence PRO83589 cDNA, wherein SEQ ID NO:170 is a clone designated herein as "DNA327559".

Figure 171 shows the amino acid sequence (SEQ ID NO:171) derived from the coding sequence of SEQ ID NO:170 shown in Figure 170.

Figure 172 shows a nucleotide sequence (SEQ ID NO:172) of a native sequence PRO83590 cDNA, wherein SEQ ID NO:172 is a clone designated herein as "DNA327560".

15       Figure 173 shows the amino acid sequence (SEQ ID NO:173) derived from the coding sequence of SEQ ID NO:172 shown in Figure 172.

Figure 174 shows a nucleotide sequence (SEQ ID NO:174) of a native sequence PRO80735 cDNA, wherein SEQ ID NO:174 is a clone designated herein as "DNA324015".

20       Figure 175 shows the amino acid sequence (SEQ ID NO:175) derived from the coding sequence of SEQ ID NO:174 shown in Figure 174.

Figure 176 shows a nucleotide sequence (SEQ ID NO:176) of a native sequence PRO36393 cDNA, wherein SEQ ID NO:176 is a clone designated herein as "DNA225930".

Figure 177 shows the amino acid sequence (SEQ ID NO:177) derived from the coding sequence of SEQ ID NO:176 shown in Figure 176.

25       Figure 178 shows a nucleotide sequence (SEQ ID NO:178) of a native sequence PRO2842 cDNA, wherein SEQ ID NO:178 is a clone designated herein as "DNA88562".

Figure 179 shows the amino acid sequence (SEQ ID NO:179) derived from the coding sequence of SEQ ID NO:178 shown in Figure 178.

30       Figure 180 shows a nucleotide sequence (SEQ ID NO:180) of a native sequence PRO81669 cDNA, wherein SEQ ID NO:180 is a clone designated herein as "DNA325092".

Figure 181 shows the amino acid sequence (SEQ ID NO:181) derived from the coding sequence of SEQ ID NO:180 shown in Figure 180.

Figure 182 shows a nucleotide sequence (SEQ ID NO:182) of a native sequence PRO49181 cDNA, wherein SEQ ID NO:182 is a clone designated herein as "DNA253582".

35       Figure 183 shows the amino acid sequence (SEQ ID NO:183) derived from the coding sequence of SEQ ID NO:182 shown in Figure 182.

Figure 184A-B shows a nucleotide sequence (SEQ ID NO:184) of a native sequence PRO83591 cDNA, wherein SEQ ID NO:184 is a clone designated herein as "DNA327561".

40       Figure 185 shows the amino acid sequence (SEQ ID NO:185) derived from the coding sequence of SEQ ID NO:184 shown in Figure 184A-B.

Figure 186 shows a nucleotide sequence (SEQ ID NO:186) of a native sequence PRO63048 cDNA, wherein SEQ ID NO:186 is a clone designated herein as "DNA275385".

Figure 187 shows the amino acid sequence (SEQ ID NO:187) derived from the coding sequence of SEQ ID NO:186 shown in Figure 186.

5        Figure 188 shows a nucleotide sequence (SEQ ID NO:188) of a native sequence PRO50067 cDNA, wherein SEQ ID NO:188 is a clone designated herein as "DNA254978".

Figure 189 shows the amino acid sequence (SEQ ID NO:189) derived from the coding sequence of SEQ ID NO:188 shown in Figure 188.

10       Figure 190 shows a nucleotide sequence (SEQ ID NO:190) of a native sequence PRO62097 cDNA, wherein SEQ ID NO:190 is a clone designated herein as "DNA274167".

Figure 191 shows the amino acid sequence (SEQ ID NO:191) derived from the coding sequence of SEQ ID NO:190 shown in Figure 190.

Figure 192A-B shows a nucleotide sequence (SEQ ID NO:192) of a native sequence cDNA, wherein SEQ ID NO:192 is a clone designated herein as "DNA327562".

15       Figure 193 shows a nucleotide sequence (SEQ ID NO:193) of a native sequence PRO80761 cDNA, wherein SEQ ID NO:193 is a clone designated herein as "DNA324044".

Figure 194 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ ID NO:193 shown in Figure 193.

20       Figure 195A-B shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO83592 cDNA, wherein SEQ ID NO:195 is a clone designated herein as "DNA327563".

Figure 196 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in Figure 195A-B.

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Figure 197 shows a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO12452 cDNA, wherein SEQ ID NO:197 is a clone designated herein as "DNA150757".

25       Figure 198 shows the amino acid sequence (SEQ ID NO:198) derived from the coding sequence of SEQ ID NO:197 shown in Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO:199) of a native sequence PRO83593 cDNA, wherein SEQ ID NO:199 is a clone designated herein as "DNA327564".

30       Figure 200 shows the amino acid sequence (SEQ ID NO:200) derived from the coding sequence of SEQ ID NO:199 shown in Figure 199.

Figure 201A-B shows a nucleotide sequence (SEQ ID NO:201) of a native sequence PRO59326 cDNA, wherein SEQ ID NO:201 is a clone designated herein as "DNA270997".

Figure 202 shows the amino acid sequence (SEQ ID NO:202) derived from the coding sequence of SEQ ID NO:201 shown in Figure 201A-B.

35       Figure 203A-B shows a nucleotide sequence (SEQ ID NO:203) of a native sequence PRO83594 cDNA, wherein SEQ ID NO:203 is a clone designated herein as "DNA327565".

Figure 204 shows the amino acid sequence (SEQ ID NO:204) derived from the coding sequence of SEQ ID NO:203 shown in Figure 203A-B.

40       Figure 205A-B shows a nucleotide sequence (SEQ ID NO:205) of a native sequence PRO83595 cDNA, wherein SEQ ID NO:205 is a clone designated herein as "DNA327566".



Figure 206 shows the amino acid sequence (SEQ ID NO:206) derived from the coding sequence of SEQ ID NO:205 shown in Figure 205A-B.

Figure 207A-B shows a nucleotide sequence (SEQ ID NO:207) of a native sequence PRO36454 cDNA, wherein SEQ ID NO:207 is a clone designated herein as "DNA225991".

5        Figure 208 shows the amino acid sequence (SEQ ID NO:208) derived from the coding sequence of SEQ ID NO:207 shown in Figure 207A-B.

Figure 209 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO83596 cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA327567".

10       Figure 210 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ ID NO:209 shown in Figure 209.

Figure 211 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO36579 cDNA, wherein SEQ ID NO:211 is a clone designated herein as "DNA226116".

Figure 212 shows the amino acid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ ID NO:211 shown in Figure 211.

15       Figure 213A-B shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO58096 cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA269686".

Figure 214 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ ID NO:213 shown in Figure 213A-B.

20       Figure 215 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO57922 cDNA, wherein SEQ ID NO:215 is a clone designated herein as "DNA327568".

Figure 216 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 215.

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Figure 217 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO2683 cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA327569".

25       Figure 218 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in Figure 217.

Figure 219 shows a nucleotide sequence (SEQ ID NO:219) of a native sequence cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA327570".

30       Figure 220 shows a nucleotide sequence (SEQ ID NO:220) of a native sequence PRO4735 cDNA, wherein SEQ ID NO:220 is a clone designated herein as "DNA327571".

Figure 221 shows the amino acid sequence (SEQ ID NO:221) derived from the coding sequence of SEQ ID NO:220 shown in Figure 220.

Figure 222 shows a nucleotide sequence (SEQ ID NO:222) of a native sequence PRO7143 cDNA, wherein SEQ ID NO:222 is a clone designated herein as "DNA129504".

35       Figure 223 shows the amino acid sequence (SEQ ID NO:223) derived from the coding sequence of SEQ ID NO:222 shown in Figure 222.

Figure 224A-B shows a nucleotide sequence (SEQ ID NO:224) of a native sequence PRO83597 cDNA, wherein SEQ ID NO:224 is a clone designated herein as "DNA327572".

40       Figure 225 shows the amino acid sequence (SEQ ID NO:225) derived from the coding sequence of SEQ ID NO:225 shown in Figure 225A-B.

Figure 226 shows a nucleotide sequence (SEQ ID NO:226) of a native sequence PRO81058 cDNA, wherein SEQ ID NO:81058 is a clone designated herein as "DNA324392".

Figure 227 shows the amino acid sequence (SEQ ID NO:227) derived from the coding sequence of SEQ ID NO:226 shown in Figure 226.

5        Figure 228 shows a nucleotide sequence (SEQ ID NO:228) of a native sequence PRO59301 cDNA, wherein SEQ ID NO:228 is a clone designated herein as "DNA327573".

Figure 229 shows the amino acid sequence (SEQ ID NO:229) derived from the coding sequence of SEQ ID NO:228 shown in Figure 228.

10       Figure 230 shows a nucleotide sequence (SEQ ID NO:230) of a native sequence PRO12878 cDNA, wherein SEQ ID NO:230 is a clone designated herein as "DNA325477".

Figure 231 shows the amino acid sequence (SEQ ID NO:231) derived from the coding sequence of SEQ ID NO:230 shown in Figure 230.

Figure 232 shows a nucleotide sequence (SEQ ID NO:232) of a native sequence PRO70994 cDNA, wherein SEQ ID NO:232 is a clone designated herein as "DNA302021".

15       Figure 233 shows the amino acid sequence (SEQ ID NO:233) derived from the coding sequence of SEQ ID NO:232 shown in Figure 232.

Figure 234 shows a nucleotide sequence (SEQ ID NO:234) of a native sequence PRO82546 cDNA, wherein SEQ ID NO:234 is a clone designated herein as "DNA326120".

20       Figure 235 shows the amino acid sequence (SEQ ID NO:235) derived from the coding sequence of SEQ ID NO:234 shown in Figure 234.

Figure 236 shows a nucleotide sequence (SEQ ID NO:236) of a native sequence PRO12478 cDNA, wherein ~~SEQ ID NO:236 is a clone designated herein as "DNA150808"~~.

Figure 237 shows the amino acid sequence (SEQ ID NO:237) derived from the coding sequence of SEQ ID NO: 236 shown in Figure 236.

25       Figure 238 shows a nucleotide sequence (SEQ ID NO:238) of a native sequence PRO59035 cDNA, wherein SEQ ID NO:238 is a clone designated herein as "DNA270669".

Figure 239 shows the amino acid sequence (SEQ ID NO:239) derived from the coding sequence of SEQ ID NO:238 shown in Figure 238.

30       Figure 240A-D shows a nucleotide sequence (SEQ ID NO:240) of a native sequence PRO83598 cDNA, wherein SEQ ID NO:240 is a clone designated herein as "DNA327574".

Figure 241 shows the amino acid sequence (SEQ ID NO:241) derived from the coding sequence of SEQ ID NO:240 shown in Figure 240A-D.

Figure 242 shows a nucleotide sequence (SEQ ID NO:242) of a native sequence PRO50174 cDNA, wherein SEQ ID NO:242 is a clone designated herein as "DNA255088".

35       Figure 243 shows the amino acid sequence (SEQ ID NO:243) derived from the coding sequence of SEQ ID NO:242 shown in Figure 242.

Figure 244A-B shows a nucleotide sequence (SEQ ID NO:244) of a native sequence PRO83599 cDNA, wherein SEQ ID NO:244 is a clone designated herein as "DNA327575".

40       Figure 245 shows the amino acid sequence (SEQ ID NO:245) derived from the coding sequence of SEQ ID NO:244 shown in Figure 244A-B.

Figure 246 shows a nucleotide sequence (SEQ ID NO:246) of a native sequence PRO81689 cDNA, wherein SEQ ID NO:246 is a clone designated herein as "DNA325115".

Figure 247 shows the amino acid sequence (SEQ ID NO:247) derived from the coding sequence of SEQ ID NO:246 shown in Figure 246.

5        Figure 248 shows a nucleotide sequence (SEQ ID NO:248) of a native sequence PRO83470 cDNA, wherein SEQ ID NO:248 is a clone designated herein as "DNA327193".

Figure 249 shows the amino acid sequence (SEQ ID NO:249) derived from the coding sequence of SEQ ID NO:248 shown in Figure 248.

10       Figure 250 shows a nucleotide sequence (SEQ ID NO:250) of a native sequence PRO58880 cDNA, wherein SEQ ID NO:250 is a clone designated herein as "DNA270502".

Figure 251 shows the amino acid sequence (SEQ ID NO:251) derived from the coding sequence of SEQ ID NO:250 shown in Figure 250.

Figure 252 shows a nucleotide sequence (SEQ ID NO:252) of a native sequence PRO12569 cDNA, wherein SEQ ID NO:252 is a clone designated herein as "DNA150989".

15       Figure 253 shows the amino acid sequence (SEQ ID NO:253) derived from the coding sequence of SEQ ID NO:252 shown in Figure 252.

Figure 254 shows a nucleotide sequence (SEQ ID NO:254) of a native sequence PRO37584 cDNA, wherein SEQ ID NO:254 is a clone designated herein as "DNA227121".

20       Figure 255 shows the amino acid sequence (SEQ ID NO:255) derived from the coding sequence of SEQ ID NO:254 shown in Figure 254.

Figure 256A-B shows a nucleotide sequence (SEQ ID NO:256) of a native sequence PRO83600 cDNA, wherein SEQ ID NO:256 is a clone designated herein as "DNA327576".

Figure 257 shows the amino acid sequence (SEQ ID NO:257) derived from the coding sequence of SEQ ID NO:256 shown in Figure 256A-B.

25       Figure 258 shows a nucleotide sequence (SEQ ID NO:258) of a native sequence PRO58089 cDNA, wherein SEQ ID NO:258 is a clone designated herein as "DNA269678".

Figure 259 shows the amino acid sequence (SEQ ID NO:259) derived from the coding sequence of SEQ ID NO:258 shown in Figure 258.

30       Figure 260 shows a nucleotide sequence (SEQ ID NO:260) of a native sequence PRO38852 cDNA, wherein SEQ ID NO:260 is a clone designated herein as "DNA234442".

Figure 261 shows the amino acid sequence (SEQ ID NO:261) derived from the coding sequence of SEQ ID NO:260 shown in Figure 260.

Figure 262A-B shows a nucleotide sequence (SEQ ID NO:262) of a native sequence PRO61835 cDNA, wherein SEQ ID NO:262 is a clone designated herein as "DNA273879".

35       Figure 263 shows the amino acid sequence (SEQ ID NO:263) derived from the coding sequence of SEQ ID NO:262 shown in Figure 262A-B

Figure 264 shows a nucleotide sequence (SEQ ID NO:264) of a native sequence PRO2113 cDNA, wherein SEQ ID NO:264 is a clone designated herein as "DNA327577".

40       Figure 265 shows the amino acid sequence (SEQ ID NO:265) derived from the coding sequence of SEQ ID NO:264 shown in Figure 264.

Figure 266A-B shows a nucleotide sequence (SEQ ID NO:266) of a native sequence PRO62605 cDNA, wherein SEQ ID NO:266 is a clone designated herein as "DNA274852".

Figure 267 shows the amino acid sequence (SEQ ID NO:267) derived from the coding sequence of SEQ ID NO:266 shown in Figure 266A-B.

5        Figure 268A-B shows a nucleotide sequence (SEQ ID NO:268) of a native sequence PRO62271 cDNA, wherein SEQ ID NO:268 is a clone designated herein as "DNA327578".

Figure 269 shows the amino acid sequence (SEQ ID NO:269) derived from the coding sequence of SEQ ID NO:268 shown in Figure 268A-B.

10       Figure 270A-C shows a nucleotide sequence (SEQ ID NO:270) of a native sequence cDNA, wherein SEQ ID NO:270 is a clone designated herein as "DNA327579".

Figure 271 shows a nucleotide sequence (SEQ ID NO:271) of a native sequence PRO83257 cDNA, wherein SEQ ID NO:271 is a clone designated herein as "DNA326939".

Figure 272 shows the amino acid sequence (SEQ ID NO:272) derived from the coding sequence of SEQ ID NO:271 shown in Figure 271.

15       Figure 273 shows a nucleotide sequence (SEQ ID NO:273) of a native sequence PRO80657 cDNA, wherein SEQ ID NO:273 is a clone designated herein as "DNA323923".

Figure 274 shows the amino acid sequence (SEQ ID NO:274) derived from the coding sequence of SEQ ID NO:273 shown in Figure 273.

20       Figure 275A-D shows a nucleotide sequence (SEQ ID NO:275) of a native sequence PRO83601 cDNA, wherein SEQ ID NO:275 is a clone designated herein as "DNA327580".

Figure 276 shows the amino acid sequence (SEQ ID NO:276) derived from the coding sequence of SEQ ID NO:275 shown in Figure 275A-D.

Figure 277A-B shows a nucleotide sequence (SEQ ID NO:277) of a native sequence PRO83602 cDNA, wherein SEQ ID NO:277 is a clone designated herein as "DNA327581".

25       Figure 278 shows the amino acid sequence (SEQ ID NO:278) derived from the coding sequence of SEQ ID NO:277 shown in Figure 277A-B.

Figure 279 shows a nucleotide sequence (SEQ ID NO:279) of a native sequence PRO2572 cDNA, wherein SEQ ID NO:279 is a clone designated herein as "DNA83058".

30       Figure 280 shows the amino acid sequence (SEQ ID NO:280) derived from the coding sequence of SEQ ID NO:279 shown in Figure 279.

Figure 281 shows a nucleotide sequence (SEQ ID NO:281) of a native sequence PRO69486 cDNA, wherein SEQ ID NO:281 is a clone designated herein as "DNA326896".

Figure 282 shows the amino acid sequence (SEQ ID NO:282) derived from the coding sequence of SEQ ID NO:281 shown in Figure 281.

35       Figure 283 shows a nucleotide sequence (SEQ ID NO:283) of a native sequence PRO82442 cDNA, wherein SEQ ID NO:283 is a clone designated herein as "DNA326000".

Figure 284 shows the amino acid sequence (SEQ ID NO:284) derived from the coding sequence of SEQ ID NO:283 shown in Figure 283.

40       Figure 285 shows a nucleotide sequence (SEQ ID NO:285) of a native sequence PRO82432 cDNA, wherein SEQ ID NO:285 is a clone designated herein as "DNA325988".

Figure 286 shows the amino acid sequence (SEQ ID NO:286) derived from the coding sequence of SEQ ID NO:285 shown in Figure 285.

Figure 287 shows a nucleotide sequence (SEQ ID NO:287) of a native sequence PRO1189 cDNA, wherein SEQ ID NO:287 is a clone designated herein as "DNA58828".

5        Figure 288 shows the amino acid sequence (SEQ ID NO:288) derived from the coding sequence of SEQ ID NO:287 shown in Figure 287.

Figure 289 shows a nucleotide sequence (SEQ ID NO:289) of a native sequence PRO1189 cDNA, wherein SEQ ID NO:289 is a clone designated herein as "DNA327192".

10       Figure 290 shows the amino acid sequence (SEQ ID NO:290) derived from the coding sequence of SEQ ID NO:289 shown in Figure 289.

Figure 291A-G shows a nucleotide sequence (SEQ ID NO:291) of a native sequence PRO83603 cDNA, wherein SEQ ID NO:291 is a clone designated herein as "DNA327582".

Figure 292 shows the amino acid sequence (SEQ ID NO:292) derived from the coding sequence of SEQ ID NO:291 shown in Figure 291A-G.

15       Figure 293 shows a nucleotide sequence (SEQ ID NO:293) of a native sequence PRO49685 cDNA, wherein SEQ ID NO:293 is a clone designated herein as "DNA254582".

Figure 294 shows the amino acid sequence (SEQ ID NO:294) derived from the coding sequence of SEQ ID NO:293 shown in Figure 293.

20       Figure 295A-B shows a nucleotide sequence (SEQ ID NO:295) of a native sequence PRO83604 cDNA, wherein SEQ ID NO:295 is a clone designated herein as "DNA327583".

Figure 296 shows the amino acid sequence (SEQ ID NO:296) derived from the coding sequence of SEQ ID NO:295 shown in Figure 295A-B.

Figure 297 shows a nucleotide sequence (SEQ ID NO:297) of a native sequence PRO59082 cDNA, wherein SEQ ID NO:297 is a clone designated herein as "DNA270719".

25       Figure 298 shows the amino acid sequence (SEQ ID NO:298) derived from the coding sequence of SEQ ID NO:297 shown in Figure 297.

Figure 299 shows a nucleotide sequence (SEQ ID NO:299) of a native sequence PRO69559 cDNA, wherein SEQ ID NO:299 is a clone designated herein as "DNA287289".

30       Figure 300 shows the amino acid sequence (SEQ ID NO:300) derived from the coding sequence of SEQ ID NO:299 shown in Figure 299.

Figure 301 shows a nucleotide sequence (SEQ ID NO:301) of a native sequence PRO61125 cDNA, wherein SEQ ID NO:301 is a clone designated herein as "DNA273060".

Figure 302 shows the amino acid sequence (SEQ ID NO:302) derived from the coding sequence of SEQ ID NO:301 shown in Figure 301.

35       Figure 303 shows a nucleotide sequence (SEQ ID NO:303) of a native sequence PRO80649 cDNA, wherein SEQ ID NO:303 is a clone designated herein as "DNA327584".

Figure 304 shows the amino acid sequence (SEQ ID NO:304) derived from the coding sequence of SEQ ID NO:303 shown in Figure 303.

40       Figure 305 shows a nucleotide sequence (SEQ ID NO:305) of a native sequence PRO12814 cDNA, wherein SEQ ID NO:305 is a clone designated herein as "DNA150872".

Figure 306 shows the amino acid sequence (SEQ ID NO:306) derived from the coding sequence of SEQ ID NO:305 shown in Figure 305.

Figure 307 shows a nucleotide sequence (SEQ ID NO:307) of a native sequence PRO83605 cDNA, wherein SEQ ID NO:307 is a clone designated herein as "DNA327585".

5        Figure 308 shows the amino acid sequence (SEQ ID NO:308) derived from the coding sequence of SEQ ID NO:307 shown in Figure 307.

Figure 309A-B shows a nucleotide sequence (SEQ ID NO:309) of a native sequence PRO24100 cDNA, wherein SEQ ID NO:309 is a clone designated herein as "DNA194837".

10       Figure 310 shows the amino acid sequence (SEQ ID NO:310) derived from the coding sequence of SEQ ID NO:309 shown in Figure 309.

Figure 311 shows a nucleotide sequence (SEQ ID NO:311) of a native sequence PRO82369 cDNA, wherein SEQ ID NO:311 is a clone designated herein as "DNA325915".

Figure 312 shows the amino acid sequence (SEQ ID NO:312) derived from the coding sequence of SEQ ID NO:311 shown in Figure 311.

15       Figure 313A-B shows a nucleotide sequence (SEQ ID NO:313) of a native sequence PRO2707 cDNA, wherein SEQ ID NO:313 is a clone designated herein as "DNA88229".

Figure 314 shows the amino acid sequence (SEQ ID NO:314) derived from the coding sequence of SEQ ID NO:313 shown in Figure 313A-B.

20       Figure 315 shows a nucleotide sequence (SEQ ID NO:315) of a native sequence PRO2579 cDNA, wherein SEQ ID NO:315 is a clone designated herein as "DNA327586".

Figure 316 shows the amino acid sequence (SEQ ID NO:316) derived from the coding sequence of ~~SEQ ID NO:315 shown in Figure 315.~~

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Figure 317 shows a nucleotide sequence (SEQ ID NO:317) of a native sequence PRO33677 cDNA, wherein SEQ ID NO:317 is a clone designated herein as "DNA210132".

25       Figure 318 shows the amino acid sequence (SEQ ID NO:318) derived from the coding sequence of SEQ ID NO:317 shown in Figure 317.

Figure 319 shows a nucleotide sequence (SEQ ID NO:319) of a native sequence PRO1720 cDNA, wherein SEQ ID NO:319 is a clone designated herein as "DNA326840".

30       Figure 320 shows the amino acid sequence (SEQ ID NO:320) derived from the coding sequence of SEQ ID NO:319 shown in Figure 319.

Figure 321 shows a nucleotide sequence (SEQ ID NO:321) of a native sequence PRO62607 cDNA, wherein SEQ ID NO:321 is a clone designated herein as "DNA324049".

Figure 322 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 321.

35       Figure 323A-B shows a nucleotide sequence (SEQ ID NO:323) of a native sequence PRO12256 cDNA, wherein SEQ ID NO:323 is a clone designated herein as "DNA150447".

Figure 324 shows the amino acid sequence (SEQ ID NO:324) derived from the coding sequence of SEQ ID NO:323 shown in Figure 323A-B.

40       Figure 325 shows a nucleotide sequence (SEQ ID NO:325) of a native sequence PRO83606 cDNA, wherein SEQ ID NO:325 is a clone designated herein as "DNA327587".

Figure 326 shows the amino acid sequence (SEQ ID NO:326) derived from the coding sequence of SEQ ID NO:325 shown in Figure 325.

Figure 327 shows a nucleotide sequence (SEQ ID NO:327) of a native sequence PRO59911 cDNA, wherein SEQ ID NO:327 is a clone designated herein as "DNA271624".

5        Figure 328 shows the amino acid sequence (SEQ ID NO:328) derived from the coding sequence of SEQ ID NO:327 shown in Figure 327.

Figure 329 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO57964 cDNA, wherein SEQ ID NO:329 is a clone designated herein as "DNA269548".

10       Figure 330 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 329.

Figure 331 shows a nucleotide sequence (SEQ ID NO:331) of a native sequence PRO83607 cDNA, wherein SEQ ID NO:331 is a clone designated herein as "DNA327588".

Figure 332 shows the amino acid sequence (SEQ ID NO:332) derived from the coding sequence of SEQ ID NO:331 shown in Figure 331.

15       Figure 333 shows a nucleotide sequence (SEQ ID NO:333) of a native sequence PRO70806 cDNA, wherein SEQ ID NO:333 is a clone designated herein as "DNA327589".

Figure 334 shows the amino acid sequence (SEQ ID NO:334) derived from the coding sequence of SEQ ID NO:333 shown in Figure 333.

20       Figure 335 shows a nucleotide sequence (SEQ ID NO:335) of a native sequence PRO2540 cDNA, wherein SEQ ID NO:335 is a clone designated herein as "DNA76514".

Figure 336 shows the amino acid sequence (SEQ ID NO:336) derived from the coding sequence of ~~SEQ ID NO:335 shown in Figure 335.~~

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Figure 337 shows a nucleotide sequence (SEQ ID NO:337) of a native sequence PRO83608 cDNA, wherein SEQ ID NO:337 is a clone designated herein as "DNA327590".

25       Figure 338 shows the amino acid sequence (SEQ ID NO:338) derived from the coding sequence of SEQ ID NO:337 shown in Figure 337.

Figure 339A-E shows a nucleotide sequence (SEQ ID NO:339) of a native sequence PRO83609 cDNA, wherein SEQ ID NO:339 is a clone designated herein as "DNA327591".

30       Figure 340 shows the amino acid sequence (SEQ ID NO:340) derived from the coding sequence of SEQ ID NO:339 shown in Figure 339A-E.

Figure 341 shows a nucleotide sequence (SEQ ID NO:341) of a native sequence PRO83610 cDNA, wherein SEQ ID NO:341 is a clone designated herein as "DNA327592".

Figure 342 shows the amino acid sequence (SEQ ID NO:342) derived from the coding sequence of SEQ ID NO:341 shown in Figure 341.

35       Figure 343 shows a nucleotide sequence (SEQ ID NO:343) of a native sequence PRO62830 cDNA, wherein SEQ ID NO:343 is a clone designated herein as "DNA287296".

Figure 344 shows the amino acid sequence (SEQ ID NO:344) derived from the coding sequence of SEQ ID NO:343 shown in Figure 343.

40       Figure 345 shows a nucleotide sequence (SEQ ID NO:345) of a native sequence PRO59733 cDNA, wherein SEQ ID NO:345 is a clone designated herein as "DNA327593".

Figure 346 shows the amino acid sequence (SEQ ID NO:346) derived from the coding sequence of SEQ ID NO:345 shown in Figure 345.

Figure 347 shows a nucleotide sequence (SEQ ID NO:347) of a native sequence PRO81169 cDNA, wherein SEQ ID NO:347 is a clone designated herein as "DNA324514".

5        Figure 348 shows the amino acid sequence (SEQ ID NO:348) derived from the coding sequence of SEQ ID NO:347 shown in Figure 347.

Figure 349 shows a nucleotide sequence (SEQ ID NO:349) of a native sequence PRO2644 cDNA, wherein SEQ ID NO:349 is a clone designated herein as "DNA88084".

10       Figure 350 shows the amino acid sequence (SEQ ID NO:350) derived from the coding sequence of SEQ ID NO:349 shown in Figure 349.

Figure 351 shows a nucleotide sequence (SEQ ID NO:351) of a native sequence PRO37015 cDNA, wherein SEQ ID NO:351 is a clone designated herein as "DNA287267".

Figure 352 shows the amino acid sequence (SEQ ID NO:352) derived from the coding sequence of SEQ ID NO:351 shown in Figure 351.

15       Figure 353 shows a nucleotide sequence (SEQ ID NO:353) of a native sequence PRO61409 cDNA, wherein SEQ ID NO:353 is a clone designated herein as "DNA273410".

Figure 354 shows the amino acid sequence (SEQ ID NO:354) derived from the coding sequence of SEQ ID NO:353 shown in Figure 353.

20       Figure 355 shows a nucleotide sequence (SEQ ID NO:355) of a native sequence PRO4798 cDNA, wherein SEQ ID NO:355 is a clone designated herein as "DNA103471".

Figure 356 shows the amino acid sequence (SEQ ID NO:356) derived from the coding sequence of ~~SEQ ID NO:355 shown in Figure 355.~~

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Figure 357A-B shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO2573 cDNA, wherein SEQ ID NO:357 is a clone designated herein as "DNA83061".

25       Figure 358 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 357A-B.

Figure 359 shows a nucleotide sequence (SEQ ID NO:359) of a native sequence PRO81936 cDNA, wherein SEQ ID NO:359 is a clone designated herein as "DNA325404".

30       Figure 360 shows the amino acid sequence (SEQ ID NO:360) derived from the coding sequence of SEQ ID NO:359 shown in Figure 359.

Figure 361 shows a nucleotide sequence (SEQ ID NO:361) of a native sequence PRO80648 cDNA, wherein SEQ ID NO:361 is a clone designated herein as "DNA323910".

Figure 362 shows the amino acid sequence (SEQ ID NO:362) derived from the coding sequence of SEQ ID NO:361 shown in Figure 361.

35       Figure 363 shows a nucleotide sequence (SEQ ID NO:363) of a native sequence PRO83611 cDNA, wherein SEQ ID NO:363 is a clone designated herein as "DNA327594".

Figure 364 shows the amino acid sequence (SEQ ID NO:364) derived from the coding sequence of SEQ ID NO:363 shown in Figure 363.

40       Figure 365 shows a nucleotide sequence (SEQ ID NO:365) of a native sequence PRO83612 cDNA, wherein SEQ ID NO:365 is a clone designated herein as "DNA327595".



Figure 366 shows the amino acid sequence (SEQ ID NO:366) derived from the coding sequence of SEQ ID NO:365 shown in Figure 365.

Figure 367A-B shows a nucleotide sequence (SEQ ID NO:367) of a native sequence PRO1920 cDNA, wherein SEQ ID NO:367 is a clone designated herein as "DNA327596".

5        Figure 368 shows the amino acid sequence (SEQ ID NO:368) derived from the coding sequence of SEQ ID NO:367 shown in Figure 367A-B.

Figure 369A-B shows a nucleotide sequence (SEQ ID NO:369) of a native sequence PRO83613 cDNA, wherein SEQ ID NO:369 is a clone designated herein as "DNA327597".

10       Figure 370 shows the amino acid sequence (SEQ ID NO:370) derived from the coding sequence of SEQ ID NO:369 shown in Figure 369A-B.

Figure 371 shows a nucleotide sequence (SEQ ID NO:371) of a native sequence PRO2831 cDNA, wherein SEQ ID NO:371 is a clone designated herein as "DNA327598".

Figure 372 shows the amino acid sequence (SEQ ID NO:372) derived from the coding sequence of SEQ ID NO:371 shown in Figure 371.

15       Figure 373A-B shows a nucleotide sequence (SEQ ID NO:373) of a native sequence PRO83614 cDNA, wherein SEQ ID NO:373 is a clone designated herein as "DNA327599".

Figure 374 shows the amino acid sequence (SEQ ID NO:374) derived from the coding sequence of SEQ ID NO:373 shown in Figure 373A-B.

20       Figure 375A-B shows a nucleotide sequence (SEQ ID NO:375) of a native sequence PRO38442 cDNA, wherein SEQ ID NO:375 is a clone designated herein as "DNA227979".

Figure 376 shows the amino acid sequence (SEQ ID NO:376) derived from the coding sequence of ~~SEQ ID NO:375 shown in Figure 375A-B.~~

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Figure 377 shows a nucleotide sequence (SEQ ID NO:377) of a native sequence PRO59478 cDNA, wherein SEQ ID NO:377 is a clone designated herein as "DNA271157".

25       Figure 378 shows the amino acid sequence (SEQ ID NO:378) derived from the coding sequence of SEQ ID NO:377 shown in Figure 377.

Figure 379 shows a nucleotide sequence (SEQ ID NO:379) of a native sequence PRO60450 cDNA, wherein SEQ ID NO:379 is a clone designated herein as "DNA272185".

30       Figure 380 shows the amino acid sequence (SEQ ID NO:380) derived from the coding sequence of SEQ ID NO:379 shown in Figure 379.

Figure 381A-B shows a nucleotide sequence (SEQ ID NO:381) of a native sequence PRO4802 cDNA, wherein SEQ ID NO:381 is a clone designated herein as "DNA103475".

Figure 382 shows the amino acid sequence (SEQ ID NO:382) derived from the coding sequence of SEQ ID NO:381 shown in Figure 381.

35       Figure 383 shows a nucleotide sequence (SEQ ID NO:383) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:383 is a clone designated herein as "DNA327600".

Figure 384 shows the amino acid sequence (SEQ ID NO:384) derived from the coding sequence of SEQ ID NO:383 shown in Figure 383 .

40       Figure 385 shows a nucleotide sequence (SEQ ID NO:385) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:385 is a clone designated herein as "DNA327601".

Figure 386 shows the amino acid sequence (SEQ ID NO:386) derived from the coding sequence of SEQ ID NO:385 shown in Figure 385.

Figure 387 shows a nucleotide sequence (SEQ ID NO:387) of a native sequence PRO61296 cDNA, wherein SEQ ID NO:387 is a clone designated herein as "DNA273286".

5        Figure 388 shows the amino acid sequence (SEQ ID NO:388) derived from the coding sequence of SEQ ID NO:387 shown in Figure 387.

Figure 389 shows a nucleotide sequence (SEQ ID NO:389) of a native sequence PRO45618 cDNA, wherein SEQ ID NO:389 is a clone designated herein as "DNA327602".

10       Figure 390 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 389.

Figure 391 shows a nucleotide sequence (SEQ ID NO:391) of a native sequence PRO58118 cDNA, wherein SEQ ID NO:391 is a clone designated herein as "DNA327603".

Figure 392 shows the amino acid sequence (SEQ ID NO:392) derived from the coding sequence of SEQ ID NO:391 shown in Figure 391.

15       Figure 393 shows a nucleotide sequence (SEQ ID NO:393) of a native sequence PRO131 cDNA, wherein SEQ ID NO:393 is a clone designated herein as "DNA53531".

Figure 394 shows the amino acid sequence (SEQ ID NO:394) derived from the coding sequence of SEQ ID NO:393 shown in Figure 393.

20       Figure 395 shows a nucleotide sequence (SEQ ID NO:395) of a native sequence PRO4728 cDNA, wherein SEQ ID NO:395 is a clone designated herein as "DNA327604".

Figure 396 shows the amino acid sequence (SEQ ID NO:396) derived from the coding sequence of SEQ ID NO:395 shown in Figure 395.

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Figure 397A-D shows a nucleotide sequence (SEQ ID NO:397) of a native sequence PRO83615 cDNA, wherein SEQ ID NO:397 is a clone designated herein as "DNA327605".

25       Figure 398A-B shows the amino acid sequence (SEQ ID NO:398) derived from the coding sequence of SEQ ID NO:397 shown in Figure 397A-D.

Figure 399A-B shows a nucleotide sequence (SEQ ID NO:399) of a native sequence PRO36600 cDNA, wherein SEQ ID NO:399 is a clone designated herein as "DNA226137".

30       Figure 400 shows the amino acid sequence (SEQ ID NO:400) derived from the coding sequence of SEQ ID NO:399 shown in Figure 399A-B.

Figure 401 shows a nucleotide sequence (SEQ ID NO:401) of a native sequence PRO57873 cDNA, wherein SEQ ID NO:401 is a clone designated herein as "DNA327606".

Figure 402 shows the amino acid sequence (SEQ ID NO:402) derived from the coding sequence of SEQ ID NO:401 shown in Figure 401.

35       Figure 403 shows a nucleotide sequence (SEQ ID NO:403) of a native sequence PRO83616 cDNA, wherein SEQ ID NO:403 is a clone designated herein as "DNA327607".

Figure 404 shows the amino acid sequence (SEQ ID NO:404) derived from the coding sequence of SEQ ID NO:403 shown in Figure 403.

40       Figure 405 shows a nucleotide sequence (SEQ ID NO:405) of a native sequence PRO62740 cDNA, wherein SEQ ID NO:405 is a clone designated herein as "DNA275012".

Figure 406 shows the amino acid sequence (SEQ ID NO:406) derived from the coding sequence of SEQ ID NO:405 shown in Figure 405.

Figure 407 shows a nucleotide sequence (SEQ ID NO:407) of a native sequence PRO83617 cDNA, wherein SEQ ID NO:407 is a clone designated herein as "DNA327608".

5        Figure 408 shows the amino acid sequence (SEQ ID NO:408) derived from the coding sequence of SEQ ID NO:407 shown in Figure 407.

Figure 409 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO36596 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "DNA226133".

10       Figure 410 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 409.

Figure 411 shows a nucleotide sequence (SEQ ID NO:411) of a native sequence PRO3629 cDNA, wherein SEQ ID NO:411 is a clone designated herein as "DNA326089".

Figure 412 shows the amino acid sequence (SEQ ID NO:412) derived from the coding sequence of SEQ ID NO:411 shown in Figure 411.

15       Figure 413 shows a nucleotide sequence (SEQ ID NO:413) of a native sequence PRO57934 cDNA, wherein SEQ ID NO:413 is a clone designated herein as "DNA269518".

Figure 414 shows the amino acid sequence (SEQ ID NO:414) derived from the coding sequence of SEQ ID NO:413 shown in Figure 413.

20       Figure 415 shows a nucleotide sequence (SEQ ID NO:415) of a native sequence PRO83618 cDNA, wherein SEQ ID NO:415 is a clone designated herein as "DNA327609".

Figure 416 shows the amino acid sequence (SEQ ID NO:416) derived from the coding sequence of SEQ ID NO:415 shown in Figure 415.

Figure 417 shows a nucleotide sequence (SEQ ID NO:417) of a native sequence PRO70595 cDNA, wherein SEQ ID NO:417 is a clone designated herein as "DNA290319".

25       Figure 418 shows the amino acid sequence (SEQ ID NO:418) derived from the coding sequence of SEQ ID NO:417 shown in Figure 417.

Figure 419 shows a nucleotide sequence (SEQ ID NO:419) of a native sequence PRO60781 cDNA, wherein SEQ ID NO:419 is a clone designated herein as "DNA272655".

30       Figure 420 shows the amino acid sequence (SEQ ID NO:420) derived from the coding sequence of SEQ ID NO:419 shown in Figure 419.

Figure 421 shows a nucleotide sequence (SEQ ID NO:421) of a native sequence PRO12186 cDNA, wherein SEQ ID NO:421 is a clone designated herein as "DNA151798".

Figure 422 shows the amino acid sequence (SEQ ID NO:422) derived from the coding sequence of SEQ ID NO:421 shown in Figure 421.

35       Figure 423 shows a nucleotide sequence (SEQ ID NO:423) of a native sequence PRO37977 cDNA, wherein SEQ ID NO:423 is a clone designated herein as "DNA227514".

Figure 424 shows the amino acid sequence (SEQ ID NO:424) derived from the coding sequence of SEQ ID NO:423 shown in Figure 423.

40       Figure 425 shows a nucleotide sequence (SEQ ID NO:425) of a native sequence PRO83619 cDNA, wherein SEQ ID NO:425 is a clone designated herein as "DNA327610".

Figure 426 shows the amino acid sequence (SEQ ID NO:426) derived from the coding sequence of SEQ ID NO:425 shown in Figure 425.

Figure 427A-B shows a nucleotide sequence (SEQ ID NO:427) of a native sequence PRO83620 cDNA, wherein SEQ ID NO:427 is a clone designated herein as "DNA327611".

5        Figure 428 shows the amino acid sequence (SEQ ID NO:428) derived from the coding sequence of SEQ ID NO:427 shown in Figure 427A-B.

Figure 429 shows a nucleotide sequence (SEQ ID NO:429) of a native sequence PRO83621 cDNA, wherein SEQ ID NO:429 is a clone designated herein as "DNA327612".

10       Figure 430 shows the amino acid sequence (SEQ ID NO:430) derived from the coding sequence of SEQ ID NO:429 shown in Figure 429.

Figure 431 shows a nucleotide sequence (SEQ ID NO:431) of a native sequence PRO82689 cDNA, wherein SEQ ID NO:431 is a clone designated herein as "DNA326287".

Figure 432 shows the amino acid sequence (SEQ ID NO:432) derived from the coding sequence of SEQ ID NO:431 shown in Figure 431.

15       Figure 433 shows a nucleotide sequence (SEQ ID NO:433) of a native sequence PRO83622 cDNA, wherein SEQ ID NO:433 is a clone designated herein as "DNA327613".

Figure 434 shows the amino acid sequence (SEQ ID NO:434) derived from the coding sequence of SEQ ID NO:433 shown in Figure 433.

20       Figure 435 shows a nucleotide sequence (SEQ ID NO:435) of a native sequence PRO11 cDNA, wherein SEQ ID NO:435 is a clone designated herein as "DNA327614".

Figure 436 shows the amino acid sequence (SEQ ID NO:436) derived from the coding sequence of ~~SEQ ID NO:435 shown in Figure 435.~~

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Figure 437A-B shows a nucleotide sequence (SEQ ID NO:437) of a native sequence PRO83623 cDNA, wherein SEQ ID NO:437 is a clone designated herein as "DNA327615".

25       Figure 438 shows the amino acid sequence (SEQ ID NO:438) derived from the coding sequence of SEQ ID NO:437 shown in Figure 437A-B.

Figure 439 shows a nucleotide sequence (SEQ ID NO:439) of a native sequence PRO83624 cDNA, wherein SEQ ID NO:439 is a clone designated herein as "DNA327616".

30       Figure 440 shows the amino acid sequence (SEQ ID NO:440) derived from the coding sequence of SEQ ID NO:439 shown in Figure 439.

Figure 441 shows a nucleotide sequence (SEQ ID NO:441) of a native sequence PRO36219 cDNA, wherein SEQ ID NO:441 is a clone designated herein as "DNA225756".

Figure 442 shows the amino acid sequence (SEQ ID NO:442) derived from the coding sequence of SEQ ID NO:441 shown in Figure 441.

35       Figure 443 shows a nucleotide sequence (SEQ ID NO:443) of a native sequence PRO4793 cDNA, wherein SEQ ID NO:443 is a clone designated herein as "DNA325800".

Figure 444 shows the amino acid sequence (SEQ ID NO:444) derived from the coding sequence of SEQ ID NO:443 shown in Figure 443.

40       Figure 445 shows a nucleotide sequence (SEQ ID NO:445) of a native sequence PRO83625 cDNA, wherein SEQ ID NO:445 is a clone designated herein as "DNA327617".

Figure 446 shows the amino acid sequence (SEQ ID NO:446) derived from the coding sequence of SEQ ID NO:445 shown in Figure 445.

Figure 447 shows a nucleotide sequence (SEQ ID NO:447) of a native sequence PRO49481 cDNA, wherein SEQ ID NO:447 is a clone designated herein as "DNA254370".

5        Figure 448 shows the amino acid sequence (SEQ ID NO:448) derived from the coding sequence of SEQ ID NO: 447 shown in Figure 447.

Figure 449A-B shows a nucleotide sequence (SEQ ID NO:449) of a native sequence PRO83626 cDNA, wherein SEQ ID NO:449 is a clone designated herein as "DNA327618".

10       Figure 450 shows the amino acid sequence (SEQ ID NO:450) derived from the coding sequence of SEQ ID NO:449 shown in Figure 449A-B .

Figure 451 shows a nucleotide sequence (SEQ ID NO:451) of a native sequence PRO83627 cDNA, wherein SEQ ID NO:451 is a clone designated herein as "DNA327619".

Figure 452 shows the amino acid sequence (SEQ ID NO:452) derived from the coding sequence of SEQ ID NO:451 shown in Figure 451.

15       Figure 453 shows a nucleotide sequence (SEQ ID NO:453) of a native sequence PRO12754 cDNA, wherein SEQ ID NO:453 is a clone designated herein as "DNA151910".

Figure 454 shows the amino acid sequence (SEQ ID NO:454) derived from the coding sequence of SEQ ID NO:453 shown in Figure 453.

20       Figure 455A-C shows a nucleotide sequence (SEQ ID NO:455) of a native sequence PRO36778 cDNA, wherein SEQ ID NO:455 is a clone designated herein as "DNA226315".

Figure 456 shows the amino acid sequence (SEQ ID NO:456) derived from the coding sequence of SEQ ID NO:455 shown in Figure 455.

Figure 457 shows a nucleotide sequence (SEQ ID NO:457) of a native sequence PRO4633 cDNA, wherein SEQ ID NO:457 is a clone designated herein as "DNA327620".

25       Figure 458 shows the amino acid sequence (SEQ ID NO:458) derived from the coding sequence of SEQ ID NO:457 shown in Figure 457.

Figure 459 shows a nucleotide sequence (SEQ ID NO:459) of a native sequence PRO83628 cDNA, wherein SEQ ID NO:459 is a clone designated herein as "DNA327621".

30       Figure 460 shows the amino acid sequence (SEQ ID NO:460) derived from the coding sequence of SEQ ID NO:459 shown in Figure 459.

Figure 461 shows a nucleotide sequence (SEQ ID NO:461) of a native sequence PRO83472 cDNA, wherein SEQ ID NO:461 is a clone designated herein as "DNA327196".

Figure 462 shows the amino acid sequence (SEQ ID NO:462) derived from the coding sequence of SEQ ID NO:461 shown in Figure 461.

35       Figure 463 shows a nucleotide sequence (SEQ ID NO:463) of a native sequence PRO83629 cDNA, wherein SEQ ID NO:463 is a clone designated herein as "DNA327622".

Figure 464 shows the amino acid sequence (SEQ ID NO:464) derived from the coding sequence of SEQ ID NO:463 shown in Figure 463.

40       Figure 465A-B shows a nucleotide sequence (SEQ ID NO:465) of a native sequence PRO12278 cDNA, wherein SEQ ID NO:465 is a clone designated herein as "DNA150475".

Figure 466 shows the amino acid sequence (SEQ ID NO:466) derived from the coding sequence of SEQ ID NO:465 shown in Figure 465A-B.

Figure 466 shows a nucleotide sequence (SEQ ID NO:466) of a native sequence PRO24089 cDNA, wherein SEQ ID NO:466 is a clone designated herein as "DNA327623".

5        Figure 467 shows the amino acid sequence (SEQ ID NO:467) derived from the coding sequence of SEQ ID NO:466 shown in Figure 466.

Figure 469 shows a nucleotide sequence (SEQ ID NO:469) of a native sequence PRO60979 cDNA, wherein SEQ ID NO:469 is a clone designated herein as "DNA272889".

10       Figure 470 shows the amino acid sequence (SEQ ID NO:470) derived from the coding sequence of SEQ ID NO:469 shown in Figure 469.

Figure 471 shows a nucleotide sequence (SEQ ID NO:471) of a native sequence PRO83630 cDNA, wherein SEQ ID NO:471 is a clone designated herein as "DNA327624".

Figure 472 shows the amino acid sequence (SEQ ID NO:472) derived from the coding sequence of SEQ ID NO:471 shown in Figure 471.

15       Figure 473 shows a nucleotide sequence (SEQ ID NO:473) of a native sequence PRO11985 cDNA, wherein SEQ ID NO:473 is a clone designated herein as "DNA151689".

Figure 474 shows the amino acid sequence (SEQ ID NO:474) derived from the coding sequence of SEQ ID NO:473 shown in Figure 473.

20       Figure 475 shows a nucleotide sequence (SEQ ID NO:475) of a native sequence PRO60900 cDNA, wherein SEQ ID NO:475 is a clone designated herein as "DNA272795".

Figure 476 shows the amino acid sequence (SEQ ID NO:476) derived from the coding sequence of ~~SEQ ID NO:475 shown in Figure 475.~~

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Figure 477 shows a nucleotide sequence (SEQ ID NO:477) of a native sequence PRO36124 cDNA, wherein SEQ ID NO:477 is a clone designated herein as "DNA225661".

25       Figure 478 shows the amino acid sequence (SEQ ID NO:478) derived from the coding sequence of SEQ ID NO:477 shown in Figure 477.

Figure 479 shows a nucleotide sequence (SEQ ID NO:479) of a native sequence PRO61634 cDNA, wherein SEQ ID NO:479 is a clone designated herein as "DNA273666".

30       Figure 480 shows the amino acid sequence (SEQ ID NO:480) derived from the coding sequence of SEQ ID NO:479 shown in Figure 479.

Figure 481 shows a nucleotide sequence (SEQ ID NO:481) of a native sequence PRO37065 cDNA, wherein SEQ ID NO:481 is a clone designated herein as "DNA226602".

Figure 482 shows the amino acid sequence (SEQ ID NO:482) derived from the coding sequence of SEQ ID NO:481 shown in Figure 481.

35       Figure 483 shows a nucleotide sequence (SEQ ID NO:483) of a native sequence PRO25138 cDNA, wherein SEQ ID NO:483 is a clone designated herein as "DNA327625".

Figure 484 shows the amino acid sequence (SEQ ID NO:484) derived from the coding sequence of SEQ ID NO:483 shown in Figure 483.

40       Figure 485 shows a nucleotide sequence (SEQ ID NO:485) of a native sequence PRO37779 cDNA, wherein SEQ ID NO:485 is a clone designated herein as "DNA327626".

Figure 486 shows the amino acid sequence (SEQ ID NO:486) derived from the coding sequence of SEQ ID NO:485 shown in Figure 485.

Figure 487 shows a nucleotide sequence (SEQ ID NO:487) of a native sequence PRO69656 cDNA, wherein SEQ ID NO:487 is a clone designated herein as "DNA287399".

5        Figure 488 shows the amino acid sequence (SEQ ID NO:488) derived from the coding sequence of SEQ ID NO:487 shown in Figure 487.

Figure 489A-B shows a nucleotide sequence (SEQ ID NO:489) of a native sequence PRO83631 cDNA, wherein SEQ ID NO:489 is a clone designated herein as "DNA327627".

10       Figure 490 shows the amino acid sequence (SEQ ID NO:490) derived from the coding sequence of SEQ ID NO:489 shown in Figure 489A-B.

Figure 491 shows a nucleotide sequence (SEQ ID NO:491) of a native sequence PRO83632 cDNA, wherein SEQ ID NO:491 is a clone designated herein as "DNA327628".

Figure 492 shows the amino acid sequence (SEQ ID NO:492) derived from the coding sequence of SEQ ID NO:491 shown in Figure 491.

15       Figure 493 shows a nucleotide sequence (SEQ ID NO:493) of a native sequence PRO83633 cDNA, wherein SEQ ID NO:493 is a clone designated herein as "DNA327629".

Figure 494 shows the amino acid sequence (SEQ ID NO:494) derived from the coding sequence of SEQ ID NO:493 shown in Figure 493.

20       Figure 495A-B shows a nucleotide sequence (SEQ ID NO:495) of a native sequence PRO36043 cDNA, wherein SEQ ID NO:495 is a clone designated herein as "DNA225580".

Figure 496 shows the amino acid sequence (SEQ ID NO:496) derived from the coding sequence of SEQ ID NO:495 shown in Figure 495A-B.

Figure 497 shows a nucleotide sequence (SEQ ID NO:497) of a native sequence PRO60569 cDNA, wherein SEQ ID NO:497 is a clone designated herein as "DNA272312".

25       Figure 498 shows the amino acid sequence (SEQ ID NO:498) derived from the coding sequence of SEQ ID NO:497 shown in Figure 497.

Figure 499 shows a nucleotide sequence (SEQ ID NO:499) of a native sequence PRO38724 cDNA, wherein SEQ ID NO:499 is a clone designated herein as "DNA327630".

30       Figure 500 shows the amino acid sequence (SEQ ID NO:500) derived from the coding sequence of SEQ ID NO:499 shown in Figure 499.

Figure 501 shows a nucleotide sequence (SEQ ID NO:501) of a native sequence PRO83634 cDNA, wherein SEQ ID NO:501 is a clone designated herein as "DNA327631".

Figure 502 shows the amino acid sequence (SEQ ID NO:502) derived from the coding sequence of SEQ ID NO:501 shown in Figure 501.

35       Figure 503 shows a nucleotide sequence (SEQ ID NO:503) of a native sequence PRO83635 cDNA, wherein SEQ ID NO:503 is a clone designated herein as "DNA327632".

Figure 504 shows the amino acid sequence (SEQ ID NO:504) derived from the coding sequence of SEQ ID NO:503 shown in Figure 503.

40       Figure 505 shows a nucleotide sequence (SEQ ID NO:505) of a native sequence PRO82726 cDNA, wherein SEQ ID NO:505 is a clone designated herein as "DNA326328".

Figure 506 shows the amino acid sequence (SEQ ID NO:506) derived from the coding sequence of SEQ ID NO:505 shown in Figure 505.

Figure 507 shows a nucleotide sequence (SEQ ID NO:507) of a native sequence PRO2870 cDNA, wherein SEQ ID NO:507 is a clone designated herein as "DNA327633".

5        Figure 508 shows the amino acid sequence (SEQ ID NO:508) derived from the coding sequence of SEQ ID NO:507 shown in Figure 507.

Figure 509 shows a nucleotide sequence (SEQ ID NO:509) of a native sequence PRO2885 cDNA, wherein SEQ ID NO:509 is a clone designated herein as "DNA88654".

10       Figure 510 shows the amino acid sequence (SEQ ID NO:510) derived from the coding sequence of SEQ ID NO:509 shown in Figure 509.

Figure 511 shows a nucleotide sequence (SEQ ID NO:511) of a native sequence PRO83636 cDNA, wherein SEQ ID NO:511 is a clone designated herein as "DNA327634".

Figure 512 shows the amino acid sequence (SEQ ID NO:512) derived from the coding sequence of SEQ ID NO:511 shown in Figure 511.

15       Figure 513 shows a nucleotide sequence (SEQ ID NO:513) of a native sequence PRO21708 cDNA, wherein SEQ ID NO:513 is a clone designated herein as "DNA188333".

Figure 514 shows the amino acid sequence (SEQ ID NO:514) derived from the coding sequence of SEQ ID NO:513 shown in Figure 513.

20       Figure 515 shows a nucleotide sequence (SEQ ID NO:515) of a native sequence PRO21825 cDNA, wherein SEQ ID NO:515 is a clone designated herein as "DNA188269".

Figure 516 shows the amino acid sequence (SEQ ID NO:516) derived from the coding sequence of SEQ ID NO:515 shown in Figure 515.

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Figure 517A-B shows a nucleotide sequence (SEQ ID NO:517) of a native sequence PRO36946 cDNA, wherein SEQ ID NO:517 is a clone designated herein as "DNA226483".

25       Figure 518 shows the amino acid sequence (SEQ ID NO:518) derived from the coding sequence of SEQ ID NO:517 shown in Figure 517A-B.

Figure 519 shows a nucleotide sequence (SEQ ID NO:519) of a native sequence PRO49203 cDNA, wherein SEQ ID NO:519 is a clone designated herein as "DNA253798".

30       Figure 520 shows the amino acid sequence (SEQ ID NO:520) derived from the coding sequence of SEQ ID NO:520 shown in Figure 520.

Figure 521 shows a nucleotide sequence (SEQ ID NO:521) of a native sequence PRO59526 cDNA, wherein SEQ ID NO:521 is a clone designated herein as "DNA271211".

Figure 522 shows the amino acid sequence (SEQ ID NO:522) derived from the coding sequence of SEQ ID NO:521 shown in Figure 521.

35       Figure 523 shows a nucleotide sequence (SEQ ID NO:523) of a native sequence PRO59946 cDNA, wherein SEQ ID NO:523 is a clone designated herein as "DNA271660".

Figure 524 shows the amino acid sequence (SEQ ID NO:524) derived from the coding sequence of SEQ ID NO:523 shown in Figure 523.

40       Figure 525 shows a nucleotide sequence (SEQ ID NO:525) of a native sequence PRO83637 cDNA, wherein SEQ ID NO:525 is a clone designated herein as "DNA327635".



Figure 526 shows the amino acid sequence (SEQ ID NO:526) derived from the coding sequence of SEQ ID NO:525 shown in Figure 525.

Figure 527 shows a nucleotide sequence (SEQ ID NO:527) of a native sequence PRO2703 cDNA, wherein SEQ ID NO:527 is a clone designated herein as "DNA88215".

5        Figure 528 shows the amino acid sequence (SEQ ID NO:528) derived from the coding sequence of SEQ ID NO:527 shown in Figure 527.

Figure 529 shows a nucleotide sequence (SEQ ID NO:529) of a native sequence PRO52392 cDNA, wherein SEQ ID NO:529 is a clone designated herein as "DNA257852".

10       Figure 530 shows the amino acid sequence (SEQ ID NO:530) derived from the coding sequence of SEQ ID NO:529 shown in Figure 529.

Figure 531 shows a nucleotide sequence (SEQ ID NO:531) of a native sequence PRO83638 cDNA, wherein SEQ ID NO:531 is a clone designated herein as "DNA327636".

Figure 532 shows the amino acid sequence (SEQ ID NO:532) derived from the coding sequence of SEQ ID NO:531 shown in Figure 531.

15       Figure 533 shows a nucleotide sequence (SEQ ID NO:533) of a native sequence PRO2552 cDNA, wherein SEQ ID NO:533 is a clone designated herein as "DNA327637".

Figure 534 shows the amino acid sequence (SEQ ID NO:534) derived from the coding sequence of SEQ ID NO:533 shown in Figure 533.

20       Figure 535 shows a nucleotide sequence (SEQ ID NO:535) of a native sequence PRO83639 cDNA, wherein SEQ ID NO:535 is a clone designated herein as "DNA327638".

Figure 536 shows the amino acid sequence (SEQ ID NO:536) derived from the coding sequence of ~~SEQ ID NO:535 shown in Figure 535.~~

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Figure 537 shows a nucleotide sequence (SEQ ID NO:537) of a native sequence PRO69600 cDNA, wherein SEQ ID NO:537 is a clone designated herein as "DNA287337".

25       Figure 538 shows the amino acid sequence (SEQ ID NO:538) derived from the coding sequence of SEQ ID NO:537 shown in Figure 537.

Figure 539 shows a nucleotide sequence (SEQ ID NO:539) of a native sequence PRO36650 cDNA, wherein SEQ ID NO:539 is a clone designated herein as "DNA226187".

30       Figure 540 shows the amino acid sequence (SEQ ID NO:540) derived from the coding sequence of SEQ ID NO:539 shown in Figure 539.

Figure 541 shows a nucleotide sequence (SEQ ID NO:541) of a native sequence PRO21885 cDNA, wherein SEQ ID NO:541 is a clone designated herein as "DNA188355".

Figure 542 shows the amino acid sequence (SEQ ID NO:542) derived from the coding sequence of SEQ ID NO:541 shown in Figure 541.

35       Figure 543 shows a nucleotide sequence (SEQ ID NO:543) of a native sequence PRO69503 cDNA, wherein SEQ ID NO:543 is a clone designated herein as "DNA287224".

Figure 544 shows the amino acid sequence (SEQ ID NO:544) derived from the coding sequence of SEQ ID NO:543 shown in Figure 543.

40       Figure 545 shows a nucleotide sequence (SEQ ID NO:545) of a native sequence PRO83640 cDNA, wherein SEQ ID NO:545 is a clone designated herein as "DNA327639".

Figure 546 shows the amino acid sequence (SEQ ID NO:546) derived from the coding sequence of SEQ ID NO:545 shown in Figure 545.

Figure 547 shows a nucleotide sequence (SEQ ID NO:547) of a native sequence PRO83641 cDNA, wherein SEQ ID NO:547 is a clone designated herein as "DNA327640".

5        Figure 548 shows the amino acid sequence (SEQ ID NO:548) derived from the coding sequence of SEQ ID NO:547 shown in Figure 547.

Figure 549 shows a nucleotide sequence (SEQ ID NO:549) of a native sequence PRO83642 cDNA, wherein SEQ ID NO:549 is a clone designated herein as "DNA327641".

10       Figure 550 shows the amino acid sequence (SEQ ID NO:550) derived from the coding sequence of SEQ ID NO:549 shown in Figure 549.

Figure 551 shows a nucleotide sequence (SEQ ID NO:551) of a native sequence PRO83643 cDNA, wherein SEQ ID NO:551 is a clone designated herein as "DNA327642".

Figure 552 shows the amino acid sequence (SEQ ID NO:552) derived from the coding sequence of SEQ ID NO:551 shown in Figure 551.

15       Figure 553 shows a nucleotide sequence (SEQ ID NO:553) of a native sequence PRO51301 cDNA, wherein SEQ ID NO:553 is a clone designated herein as "DNA256257".

Figure 554 shows the amino acid sequence (SEQ ID NO:554) derived from the coding sequence of SEQ ID NO:553 shown in Figure 553.

20       Figure 555A-B shows a nucleotide sequence (SEQ ID NO:555) of a native sequence PRO83644 cDNA, wherein SEQ ID NO:555 is a clone designated herein as "DNA327643".

Figure 556 shows the amino acid sequence (SEQ ID NO:556) derived from the coding sequence of SEQ ID NO:555 shown in Figure 555A-B.

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Figure 557 shows a nucleotide sequence (SEQ ID NO:557) of a native sequence PRO2267 cDNA, wherein SEQ ID NO:557 is a clone designated herein as "DNA88281".

25       Figure 558 shows the amino acid sequence (SEQ ID NO:558) derived from the coding sequence of SEQ ID NO:557 shown in Figure 557.

Figure 559 shows a nucleotide sequence (SEQ ID NO:559) of a native sequence PRO81000 cDNA, wherein SEQ ID NO:559 is a clone designated herein as "DNA324324".

30       Figure 560 shows the amino acid sequence (SEQ ID NO:560) derived from the coding sequence of SEQ ID NO:559 shown in Figure 559.

Figure 561 shows a nucleotide sequence (SEQ ID NO:561) of a native sequence PRO69582 cDNA, wherein SEQ ID NO:561 is a clone designated herein as "DNA287317".

Figure 562 shows the amino acid sequence (SEQ ID NO:562) derived from the coding sequence of SEQ ID NO:561 shown in Figure 561.

35       Figure 563 shows a nucleotide sequence (SEQ ID NO:563) of a native sequence PRO83645 cDNA, wherein SEQ ID NO:563 is a clone designated herein as "DNA327644".

Figure 564 shows the amino acid sequence (SEQ ID NO:564) derived from the coding sequence of SEQ ID NO:563 shown in Figure 563.

40       Figure 565 shows a nucleotide sequence (SEQ ID NO:565) of a native sequence PRO2715 cDNA, wherein SEQ ID NO:565 is a clone designated herein as "DNA88248".

Figure 566 shows the amino acid sequence (SEQ ID NO:566) derived from the coding sequence of SEQ ID NO:565 shown in Figure 565.

Figure 567 shows a nucleotide sequence (SEQ ID NO:567) of a native sequence PRO83646 cDNA, wherein SEQ ID NO:567 is a clone designated herein as "DNA327645".

5        Figure 568 shows the amino acid sequence (SEQ ID NO:568) derived from the coding sequence of SEQ ID NO:567 shown in Figure 567.

Figure 569 shows a nucleotide sequence (SEQ ID NO:569) of a native sequence PRO83647 cDNA, wherein SEQ ID NO:569 is a clone designated herein as "DNA327646".

10       Figure 570 shows the amino acid sequence (SEQ ID NO:570) derived from the coding sequence of SEQ ID NO:569 shown in Figure 569.

Figure 571A-B shows a nucleotide sequence (SEQ ID NO:571) of a native sequence PRO12449 cDNA, wherein SEQ ID NO:571 is a clone designated herein as "DNA226859".

Figure 572 shows the amino acid sequence (SEQ ID NO:572) derived from the coding sequence of SEQ ID NO:571 shown in Figure 571A-B.

15       Figure 573 shows a nucleotide sequence (SEQ ID NO:573) of a native sequence PRO36372 cDNA, wherein SEQ ID NO:573 is a clone designated herein as "DNA225909".

Figure 574 shows the amino acid sequence (SEQ ID NO:574) derived from the coding sequence of SEQ ID NO:573 shown in Figure 573.

20       Figure 575 shows a nucleotide sequence (SEQ ID NO:575) of a native sequence PRO2447 cDNA, wherein SEQ ID NO:575 is a clone designated herein as "DNA327647".

Figure 576 shows the amino acid sequence (SEQ ID NO:576) derived from the coding sequence of SEQ ID NO:575 shown in Figure 575.

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Figure 577 shows a nucleotide sequence (SEQ ID NO:577) of a native sequence PRO83648 cDNA, wherein SEQ ID NO:577 is a clone designated herein as "DNA327648".

25       Figure 578 shows the amino acid sequence (SEQ ID NO:578) derived from the coding sequence of SEQ ID NO:577 shown in Figure 577.

Figure 579A-B shows a nucleotide sequence (SEQ ID NO:579) of a native sequence PRO4673 cDNA, wherein SEQ ID NO:579 is a clone designated herein as "DNA327649".

30       Figure 580 shows the amino acid sequence (SEQ ID NO:580) derived from the coding sequence of SEQ ID NO:579 shown in Figure 579A-B.

Figure 581 shows a nucleotide sequence (SEQ ID NO:581) of a native sequence PRO12489 cDNA, wherein SEQ ID NO:581 is a clone designated herein as "DNA150830".

Figure 582 shows the amino acid sequence (SEQ ID NO:582) derived from the coding sequence of SEQ ID NO:581 shown in Figure 581.

35       Figure 583 shows a nucleotide sequence (SEQ ID NO:583) of a native sequence PRO36008 cDNA, wherein SEQ ID NO:583 is a clone designated herein as "DNA327650".

Figure 584 shows the amino acid sequence (SEQ ID NO:584) derived from the coding sequence of SEQ ID NO:583 shown in Figure 583.

40       Figure 585 shows a nucleotide sequence (SEQ ID NO:585) of a native sequence PRO83649 cDNA, wherein SEQ ID NO:585 is a clone designated herein as "DNA327651".

Figure 586 shows the amino acid sequence (SEQ ID NO:586) derived from the coding sequence of SEQ ID NO:585 shown in Figure 585.

Figure 587 shows a nucleotide sequence (SEQ ID NO:587) of a native sequence PRO70423 cDNA, wherein SEQ ID NO:587 is a clone designated herein as "DNA290279".

5 Figure 588 shows the amino acid sequence (SEQ ID NO:588) derived from the coding sequence of SEQ ID NO:587 shown in Figure 587.

Figure 589A-B shows a nucleotide sequence (SEQ ID NO:589) of a native sequence PRO50365 cDNA, wherein SEQ ID NO:589 is a clone designated herein as "DNA255292".

10 Figure 590 shows the amino acid sequence (SEQ ID NO:590) derived from the coding sequence of SEQ ID NO:589 shown in Figure 589A-B.

Figure 591 shows a nucleotide sequence (SEQ ID NO:591) of a native sequence PRO58149 cDNA, wherein SEQ ID NO:591 is a clone designated herein as "DNA269740".

Figure 592 shows the amino acid sequence (SEQ ID NO:592) derived from the coding sequence of SEQ ID NO:591 shown in Figure 591.

15 Figure 593A-B shows a nucleotide sequence (SEQ ID NO:593) of a native sequence PRO2628 cDNA, wherein SEQ ID NO:593 is a clone designated herein as "DNA327652".

Figure 594 shows the amino acid sequence (SEQ ID NO:594) derived from the coding sequence of SEQ ID NO:593 shown in Figure 593A-B.

20 Figure 595 shows a nucleotide sequence (SEQ ID NO:595) of a native sequence PRO49580 cDNA, wherein SEQ ID NO:595 is a clone designated herein as "DNA254472".

Figure 596 shows the amino acid sequence (SEQ ID NO:596) derived from the coding sequence of ~~SEQ ID NO:595 shown in Figure 595.~~

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Figure 597 shows a nucleotide sequence (SEQ ID NO:597) of a native sequence PRO59596 cDNA, wherein SEQ ID NO:597 is a clone designated herein as "DNA327653".

25 Figure 598 shows the amino acid sequence (SEQ ID NO:598) derived from the coding sequence of SEQ ID NO:597 shown in Figure 597.

Figure 599 shows a nucleotide sequence (SEQ ID NO:599) of a native sequence PRO59210 cDNA, wherein SEQ ID NO:599 is a clone designated herein as "DNA270875".

30 Figure 600 shows the amino acid sequence (SEQ ID NO:600) derived from the coding sequence of SEQ ID NO:599 shown in Figure 599.

Figure 601A-B shows a nucleotide sequence (SEQ ID NO:601) of a native sequence PRO70395 cDNA, wherein SEQ ID NO:601 is a clone designated herein as "DNA290265".

Figure 602 shows the amino acid sequence (SEQ ID NO:602) derived from the coding sequence of SEQ ID NO:601 shown in Figure 601A-B.

35 Figure 603 shows a nucleotide sequence (SEQ ID NO:603) of a native sequence PRO58792 cDNA, wherein SEQ ID NO:603 is a clone designated herein as "DNA270411".

Figure 604 shows the amino acid sequence (SEQ ID NO:604) derived from the coding sequence of SEQ ID NO:603 shown in Figure 603.

40 Figure 605 shows a nucleotide sequence (SEQ ID NO:605) of a native sequence PRO83650 cDNA, wherein SEQ ID NO:605 is a clone designated herein as "DNA327654".

Figure 606 shows the amino acid sequence (SEQ ID NO:606) derived from the coding sequence of SEQ ID NO:605 shown in Figure 605.

Figure 607 shows a nucleotide sequence (SEQ ID NO:607) of a native sequence PRO322 cDNA, wherein SEQ ID NO:607 is a clone designated herein as "DNA327655".

5        Figure 608 shows the amino acid sequence (SEQ ID NO:608) derived from the coding sequence of SEQ ID NO:607 shown in Figure 607.

Figure 609 shows a nucleotide sequence (SEQ ID NO:609) of a native sequence PRO69572 cDNA, wherein SEQ ID NO:609 is a clone designated herein as "DNA287306".

10       Figure 610 shows the amino acid sequence (SEQ ID NO:610) derived from the coding sequence of SEQ ID NO:609 shown in Figure 609.

Figure 611 shows a nucleotide sequence (SEQ ID NO:611) of a native sequence PRO36117 cDNA, wherein SEQ ID NO:611 is a clone designated herein as "DNA327656".

Figure 612 shows the amino acid sequence (SEQ ID NO:612) derived from the coding sequence of SEQ ID NO:611 shown in Figure 611.

15       Figure 613 shows a nucleotide sequence (SEQ ID NO:613) of a native sequence PRO59399 cDNA, wherein SEQ ID NO:613 is a clone designated herein as "DNA271075".

Figure 614 shows the amino acid sequence (SEQ ID NO:614) derived from the coding sequence of SEQ ID NO:613 shown in Figure 613.

20       Figure 615A-B shows a nucleotide sequence (SEQ ID NO:615) of a native sequence PRO38147 cDNA, wherein SEQ ID NO:615 is a clone designated herein as "DNA327657".

Figure 616 shows the amino acid sequence (SEQ ID NO:616) derived from the coding sequence of ~~SEQ ID NO:615 shown in Figure 615.~~

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Figure 617 shows a nucleotide sequence (SEQ ID NO:617) of a native sequence PRO83651 cDNA, wherein SEQ ID NO:617 is a clone designated herein as "DNA327658".

25       Figure 618 shows the amino acid sequence (SEQ ID NO:618) derived from the coding sequence of SEQ ID NO:617 shown in Figure 617.

Figure 619 shows a nucleotide sequence (SEQ ID NO:619) of a native sequence PRO36302 cDNA, wherein SEQ ID NO:619 is a clone designated herein as "DNA225839".

30       Figure 620 shows the amino acid sequence (SEQ ID NO:620) derived from the coding sequence of SEQ ID NO:619 shown in Figure 619.

Figure 621 shows a nucleotide sequence (SEQ ID NO:621) of a native sequence PRO70443 cDNA, wherein SEQ ID NO:621 is a clone designated herein as "DNA327659".

Figure 622 shows the amino acid sequence (SEQ ID NO:622) derived from the coding sequence of SEQ ID NO:621 shown in Figure 621.

35       Figure 623 shows a nucleotide sequence (SEQ ID NO:623) of a native sequence PRO2063 cDNA, wherein SEQ ID NO:623 is a clone designated herein as "DNA83055".

Figure 624 shows the amino acid sequence (SEQ ID NO:624) derived from the coding sequence of SEQ ID NO:623 shown in Figure 623.

40       Figure 625 shows a nucleotide sequence (SEQ ID NO:625) of a native sequence PRO327 cDNA, wherein SEQ ID NO:625 is a clone designated herein as "DNA327660".

Figure 626 shows the amino acid sequence (SEQ ID NO:626) derived from the coding sequence of SEQ ID NO:625 shown in Figure 625.

Figure 627 shows a nucleotide sequence (SEQ ID NO:627) of a native sequence PRO83652 cDNA, wherein SEQ ID NO:627 is a clone designated herein as "DNA327661".

5        Figure 628 shows the amino acid sequence (SEQ ID NO:628) derived from the coding sequence of SEQ ID NO:627 shown in Figure 627.

Figure 629 shows a nucleotide sequence (SEQ ID NO:629) of a native sequence PRO36992 cDNA, wherein SEQ ID NO:629 is a clone designated herein as "DNA299878".

10       Figure 630 shows the amino acid sequence (SEQ ID NO:630) derived from the coding sequence of SEQ ID NO:629 shown in Figure 629.

Figure 631 shows a nucleotide sequence (SEQ ID NO:631) of a native sequence PRO2018 cDNA, wherein SEQ ID NO:631 is a clone designated herein as "DNA75863".

Figure 632 shows the amino acid sequence (SEQ ID NO:632) derived from the coding sequence of SEQ ID NO:631 shown in Figure 631.

15       Figure 633 shows a nucleotide sequence (SEQ ID NO:633) of a native sequence PRO38396 cDNA, wherein SEQ ID NO:633 is a clone designated herein as "DNA227933".

Figure 634 shows the amino acid sequence (SEQ ID NO:634) derived from the coding sequence of SEQ ID NO:633 shown in Figure 633.

20       Figure 635A-B shows a nucleotide sequence (SEQ ID NO:635) of a native sequence cDNA, wherein SEQ ID NO:635 is a clone designated herein as "DNA327662".

Figure 636 shows a nucleotide sequence (SEQ ID NO:636) of a native sequence PRO37683 cDNA, wherein SEQ ID NO:636 is a clone designated herein as "DNA227220".

Figure 637 shows the amino acid sequence (SEQ ID NO:637) derived from the coding sequence of SEQ ID NO:636 shown in Figure 636.

25       Figure 638 shows a nucleotide sequence (SEQ ID NO:638) of a native sequence PRO35062 cDNA, wherein SEQ ID NO:638 is a clone designated herein as "DNA213596".

Figure 639 shows the amino acid sequence (SEQ ID NO:639) derived from the coding sequence of SEQ ID NO:638 shown in Figure 638.

30       Figure 640 shows a nucleotide sequence (SEQ ID NO:640) of a native sequence PRO81618 cDNA, wherein SEQ ID NO:640 is a clone designated herein as "DNA325029".

Figure 641 shows the amino acid sequence (SEQ ID NO:641) derived from the coding sequence of SEQ ID NO:640 shown in Figure 640.

Figure 642 shows a nucleotide sequence (SEQ ID NO:642) of a native sequence PRO83654 cDNA, wherein SEQ ID NO:642 is a clone designated herein as "DNA327663".

35       Figure 643 shows the amino acid sequence (SEQ ID NO:643) derived from the coding sequence of SEQ ID NO:642 shown in Figure 642.

Figure 644 shows a nucleotide sequence (SEQ ID NO:644) of a native sequence PRO2722 cDNA, wherein SEQ ID NO:644 is a clone designated herein as "DNA327664".

40       Figure 645 shows the amino acid sequence (SEQ ID NO:645) derived from the coding sequence of SEQ ID NO:644 shown in Figure 644.

Figure 646 shows a nucleotide sequence (SEQ ID NO:646) of a native sequence PRO38104 cDNA, wherein SEQ ID NO:646 is a clone designated herein as "DNA227641".

Figure 647 shows the amino acid sequence (SEQ ID NO:647) derived from the coding sequence of SEQ ID NO:646 shown in Figure 646.

5        Figure 648 shows a nucleotide sequence (SEQ ID NO:648) of a native sequence PRO83655 cDNA, wherein SEQ ID NO:648 is a clone designated herein as "DNA327665".

Figure 649 shows the amino acid sequence (SEQ ID NO:649) derived from the coding sequence of SEQ ID NO:650 shown in Figure 650.

10       Figure 650 shows a nucleotide sequence (SEQ ID NO:650) of a native sequence PRO83656 cDNA, wherein SEQ ID NO:650 is a clone designated herein as "DNA327666".

Figure 651 shows the amino acid sequence (SEQ ID NO:651) derived from the coding sequence of SEQ ID NO:650 shown in Figure 650.

Figure 652 shows a nucleotide sequence (SEQ ID NO:652) of a native sequence PRO83135 cDNA, wherein SEQ ID NO:652 is a clone designated herein as "DNA327667".

15       Figure 653 shows the amino acid sequence (SEQ ID NO:653) derived from the coding sequence of SEQ ID NO:652 shown in Figure 652.

Figure 654 shows a nucleotide sequence (SEQ ID NO:654) of a native sequence PRO83141 cDNA, wherein SEQ ID NO:654 is a clone designated herein as "DNA327668".

20       Figure 655 shows the amino acid sequence (SEQ ID NO:655) derived from the coding sequence of SEQ ID NO:654 shown in Figure 654.

Figure 656 shows a nucleotide sequence (SEQ ID NO:656) of a native sequence PRO83657 cDNA, wherein SEQ ID NO:656 is a clone designated herein as "DNA327669".

Figure 657 shows the amino acid sequence (SEQ ID NO:657) derived from the coding sequence of SEQ ID NO:656 shown in Figure 656.

25       Figure 658 shows a nucleotide sequence (SEQ ID NO:658) of a native sequence PRO1288 cDNA, wherein SEQ ID NO:658 is a clone designated herein as "DNA327670".

Figure 659 shows the amino acid sequence (SEQ ID NO:659) derived from the coding sequence of SEQ ID NO:658 shown in Figure 658.

30       Figure 660 shows a nucleotide sequence (SEQ ID NO:660) of a native sequence PRO83658 cDNA, wherein SEQ ID NO:660 is a clone designated herein as "DNA327671".

Figure 661 shows the amino acid sequence (SEQ ID NO:661) derived from the coding sequence of SEQ ID NO:660 shown in Figure 660.

Figure 662 shows a nucleotide sequence (SEQ ID NO:662) of a native sequence PRO2200 cDNA, wherein SEQ ID NO:662 is a clone designated herein as "DNA88155".

35       Figure 663 shows the amino acid sequence (SEQ ID NO:663) derived from the coding sequence of SEQ ID NO:662 shown in Figure 662.

Figure 664 shows a nucleotide sequence (SEQ ID NO:664) of a native sequence PRO58669 cDNA, wherein SEQ ID NO:664 is a clone designated herein as "DNA270281".

40       Figure 665 shows the amino acid sequence (SEQ ID NO:665) derived from the coding sequence of SEQ ID NO:664 shown in Figure 664.

Figure 666 shows a nucleotide sequence (SEQ ID NO:666) of a native sequence PRO83659 cDNA, wherein SEQ ID NO:666 is a clone designated herein as "DNA327672".

Figure 667 shows the amino acid sequence (SEQ ID NO:667) derived from the coding sequence of SEQ ID NO:666 shown in Figure 666.

5        Figure 668 shows a nucleotide sequence (SEQ ID NO:668) of a native sequence PRO21820 cDNA, wherein SEQ ID NO:668 is a clone designated herein as "DNA188289".

Figure 669 shows the amino acid sequence (SEQ ID NO:669) derived from the coding sequence of SEQ ID NO:668 shown in Figure 668.

10       Figure 670 shows a nucleotide sequence (SEQ ID NO:670) of a native sequence PRO37994 cDNA, wherein SEQ ID NO:670 is a clone designated herein as "DNA227531".

Figure 671 shows the amino acid sequence (SEQ ID NO:671) derived from the coding sequence of SEQ ID NO:670 shown in Figure 670.

Figure 672 shows a nucleotide sequence (SEQ ID NO:672) of a native sequence PRO83660 cDNA, wherein SEQ ID NO:672 is a clone designated herein as "DNA327673".

15       Figure 673 shows the amino acid sequence (SEQ ID NO:673) derived from the coding sequence of SEQ ID NO:672 shown in Figure 672.

Figure 674A-B shows a nucleotide sequence (SEQ ID NO:674) of a native sequence PRO83661 cDNA, wherein SEQ ID NO:674 is a clone designated herein as "DNA327674".

20       Figure 675 shows the amino acid sequence (SEQ ID NO:675) derived from the coding sequence of SEQ ID NO:674 shown in Figure 674A-B.

Figure 676 shows a nucleotide sequence (SEQ ID NO:676) of a native sequence PRO83662 cDNA, wherein SEQ ID NO:676 is a clone designated herein as "DNA327675".

Figure 677 shows the amino acid sequence (SEQ ID NO:677) derived from the coding sequence of SEQ ID NO:676 shown in Figure 676.

25       Figure 678 shows a nucleotide sequence (SEQ ID NO:678) of a native sequence PRO2040 cDNA, wherein SEQ ID NO:678 is a clone designated herein as "DNA327676".

Figure 679 shows the amino acid sequence (SEQ ID NO:679) derived from the coding sequence of SEQ ID NO:678 shown in Figure 678.

30       Figure 680A-B shows a nucleotide sequence (SEQ ID NO:680) of a native sequence PRO50849 cDNA, wherein SEQ ID NO:680 is a clone designated herein as "DNA255794".

Figure 681 shows the amino acid sequence (SEQ ID NO:681) derived from the coding sequence of SEQ ID NO:680 shown in Figure 680.

Figure 682 shows a nucleotide sequence (SEQ ID NO:682) of a native sequence PRO50985 cDNA, wherein SEQ ID NO:682 is a clone designated herein as "DNA255933".

35       Figure 683 shows the amino acid sequence (SEQ ID NO:683) derived from the coding sequence of SEQ ID NO:682 shown in Figure 682.

Figure 684 shows a nucleotide sequence (SEQ ID NO:684) of a native sequence PRO50904 cDNA, wherein SEQ ID NO:684 is a clone designated herein as "DNA255850".

40       Figure 685 shows the amino acid sequence (SEQ ID NO:685) derived from the coding sequence of SEQ ID NO:684 shown in Figure 684.



Figure 686 shows a nucleotide sequence (SEQ ID NO:686) of a native sequence PRO38131 cDNA, wherein SEQ ID NO:686 is a clone designated herein as "DNA227668".

Figure 687 shows the amino acid sequence (SEQ ID NO:687) derived from the coding sequence of SEQ ID NO:686 shown in Figure 686.

5        Figure 688 shows a nucleotide sequence (SEQ ID NO:688) of a native sequence PRO24015 cDNA, wherein SEQ ID NO:688 is a clone designated herein as "DNA327677".

Figure 689 shows the amino acid sequence (SEQ ID NO:689) derived from the coding sequence of SEQ ID NO:688 shown in Figure 688.

10       Figure 690 shows a nucleotide sequence (SEQ ID NO:690) of a native sequence PRO35066 cDNA, wherein SEQ ID NO:690 is a clone designated herein as "DNA327678".

Figure 691 shows the amino acid sequence (SEQ ID NO:691) derived from the coding sequence of SEQ ID NO:690 shown in Figure 690.

Figure 692 shows a nucleotide sequence (SEQ ID NO:692) of a native sequence PRO23864 cDNA, wherein SEQ ID NO:692 is a clone designated herein as "DNA194506".

15       Figure 693 shows the amino acid sequence (SEQ ID NO:693) derived from the coding sequence of SEQ ID NO:692 shown in Figure 692.

Figure 694 shows a nucleotide sequence (SEQ ID NO:694) of a native sequence PRO83663 cDNA, wherein SEQ ID NO:694 is a clone designated herein as "DNA327679".

20       Figure 695 shows the amino acid sequence (SEQ ID NO:695) derived from the coding sequence of SEQ ID NO:694 shown in Figure 694.

Figure 696 shows a nucleotide sequence (SEQ ID NO:696) of a native sequence PRO83664 cDNA, wherein SEQ ID NO:696 is a clone designated herein as "DNA327680".

Figure 697 shows the amino acid sequence (SEQ ID NO:697) derived from the coding sequence of SEQ ID NO:696 shown in Figure 696.

25       Figure 698A-C shows a nucleotide sequence (SEQ ID NO:698) of a native sequence PRO83665 cDNA, wherein SEQ ID NO:698 is a clone designated herein as "DNA327681".

Figure 699 shows the amino acid sequence (SEQ ID NO:699) derived from the coding sequence of SEQ ID NO:698 shown in Figure 698A-C.

30       Figure 700 shows a nucleotide sequence (SEQ ID NO:700) of a native sequence PRO83666 cDNA, wherein SEQ ID NO:700 is a clone designated herein as "DNA327682".

Figure 701 shows the amino acid sequence (SEQ ID NO:701) derived from the coding sequence of SEQ ID NO:700 shown in Figure 700.

Figure 702 shows a nucleotide sequence (SEQ ID NO:702) of a native sequence PRO58590 cDNA, wherein SEQ ID NO:702 is a clone designated herein as "DNA270202".

35       Figure 703 shows the amino acid sequence (SEQ ID NO:703) derived from the coding sequence of SEQ ID NO:702 shown in Figure 702.

Figure 704 shows a nucleotide sequence (SEQ ID NO:704) of a native sequence PRO83667 cDNA, wherein SEQ ID NO:704 is a clone designated herein as "DNA327683".

40       Figure 705 shows the amino acid sequence (SEQ ID NO:705) derived from the coding sequence of SEQ ID NO:704 shown in Figure 704.

Figure 706A-B shows a nucleotide sequence (SEQ ID NO:706) of a native sequence PRO83668 cDNA, wherein SEQ ID NO:706 is a clone designated herein as "DNA327684".

Figure 707 shows the amino acid sequence (SEQ ID NO:707) derived from the coding sequence of SEQ ID NO:706 shown in Figure 706A-B.

5        Figure 708 shows a nucleotide sequence (SEQ ID NO:708) of a native sequence PRO83669 cDNA, wherein SEQ ID NO:708 is a clone designated herein as "DNA327685".

Figure 709 shows the amino acid sequence (SEQ ID NO:709) derived from the coding sequence of SEQ ID NO:708 shown in Figure 708.

10       Figure 710 shows a nucleotide sequence (SEQ ID NO:710) of a native sequence PRO83670 cDNA, wherein SEQ ID NO:710 is a clone designated herein as "DNA327686".

Figure 711 shows the amino acid sequence (SEQ ID NO:711) derived from the coding sequence of SEQ ID NO:710 shown in Figure 710.

Figure 712 shows a nucleotide sequence (SEQ ID NO:712) of a native sequence PRO83671 cDNA, wherein SEQ ID NO:712 is a clone designated herein as "DNA327687".

15       Figure 713 shows the amino acid sequence (SEQ ID NO:713) derived from the coding sequence of SEQ ID NO:712 shown in Figure 712.

Figure 714 shows a nucleotide sequence (SEQ ID NO:714) of a native sequence PRO83672 cDNA, wherein SEQ ID NO:714 is a clone designated herein as "DNA327688".

20       Figure 715 shows the amino acid sequence (SEQ ID NO:715) derived from the coding sequence of SEQ ID NO:714 shown in Figure 714.

Figure 716A-B shows a nucleotide sequence (SEQ ID NO:716) of a native sequence PRO82391 cDNA, wherein SEQ ID NO:716 is a clone designated herein as "DNA325944".

Figure 717 shows the amino acid sequence (SEQ ID NO:717) derived from the coding sequence of SEQ ID NO:716 shown in Figure 716A-B.

25       Figure 718 shows a nucleotide sequence (SEQ ID NO:718) of a native sequence PRO9824 cDNA, wherein SEQ ID NO:718 is a clone designated herein as "DNA327689".

Figure 719 shows the amino acid sequence (SEQ ID NO:719) derived from the coding sequence of SEQ ID NO:718 shown in Figure 718.

30       Figure 720 shows a nucleotide sequence (SEQ ID NO:720) of a native sequence PRO83673 cDNA, wherein SEQ ID NO:720 is a clone designated herein as "DNA327690".

Figure 721 shows the amino acid sequence (SEQ ID NO:721) derived from the coding sequence of SEQ ID NO:720 shown in Figure 720.

Figure 722 shows a nucleotide sequence (SEQ ID NO:722) of a native sequence PRO83674 cDNA, wherein SEQ ID NO:722 is a clone designated herein as "DNA327691".

35       Figure 723 shows the amino acid sequence (SEQ ID NO:723) derived from the coding sequence of SEQ ID NO:722 shown in Figure 722.

Figure 724 shows a nucleotide sequence (SEQ ID NO:724) of a native sequence PRO83675 cDNA, wherein SEQ ID NO:724 is a clone designated herein as "DNA327692".

40       Figure 725 shows the amino acid sequence (SEQ ID NO:725) derived from the coding sequence of SEQ ID NO:724 shown in Figure 724.

Figure 726A-C shows a nucleotide sequence (SEQ ID NO:726) of a native sequence PRO83676 cDNA, wherein SEQ ID NO:726 is a clone designated herein as "DNA327693".

Figure 727 shows the amino acid sequence (SEQ ID NO:727) derived from the coding sequence of SEQ ID NO:726 shown in Figure 726A-C.

5        Figure 728A-C shows a nucleotide sequence (SEQ ID NO:728) of a native sequence PRO83677 cDNA, wherein SEQ ID NO:728 is a clone designated herein as "DNA327694".

Figure 729 shows the amino acid sequence (SEQ ID NO:729) derived from the coding sequence of SEQ ID NO:728 shown in Figure 728A-C.

10       Figure 730A-C shows a nucleotide sequence (SEQ ID NO:730) of a native sequence PRO83678 cDNA, wherein SEQ ID NO:730 is a clone designated herein as "DNA327695".

Figure 731 shows the amino acid sequence (SEQ ID NO:731) derived from the coding sequence of SEQ ID NO:730 shown in Figure 730A-C.

Figure 732A-B shows a nucleotide sequence (SEQ ID NO:732) of a native sequence PRO4870 cDNA, wherein SEQ ID NO:732 is a clone designated herein as "DNA325513".

15       Figure 733 shows the amino acid sequence (SEQ ID NO:733) derived from the coding sequence of SEQ ID NO:732 shown in Figure 732A-B.

Figure 734 shows a nucleotide sequence (SEQ ID NO:734) of a native sequence PRO83679 cDNA, wherein SEQ ID NO:734 is a clone designated herein as "DNA327696".

20       Figure 735 shows the amino acid sequence (SEQ ID NO:735) derived from the coding sequence of SEQ ID NO:734 shown in Figure 734.

Figure 736 shows a nucleotide sequence (SEQ ID NO:736) of a native sequence PRO62376 cDNA, wherein SEQ ID NO:736 is a clone designated herein as "DNA274471".

Figure 737 shows the amino acid sequence (SEQ ID NO:737) derived from the coding sequence of SEQ ID NO:736 shown in Figure 736.

25       Figure 738 shows a nucleotide sequence (SEQ ID NO:738) of a native sequence PRO83680 cDNA, wherein SEQ ID NO:738 is a clone designated herein as "DNA327697".

Figure 739 shows the amino acid sequence (SEQ ID NO:739) derived from the coding sequence of SEQ ID NO:738 shown in Figure 738.

30       Figure 740 shows a nucleotide sequence (SEQ ID NO:740) of a native sequence PRO83681 cDNA, wherein SEQ ID NO:740 is a clone designated herein as "DNA327698".

Figure 741 shows the amino acid sequence (SEQ ID NO:741) derived from the coding sequence of SEQ ID NO:740 shown in Figure 740.

Figure 742 shows a nucleotide sequence (SEQ ID NO:742) of a native sequence PRO83682 cDNA, wherein SEQ ID NO:742 is a clone designated herein as "DNA327699".

35       Figure 743 shows the amino acid sequence (SEQ ID NO:743) derived from the coding sequence of SEQ ID NO:742 shown in Figure 742.

Figure 744A-B shows a nucleotide sequence (SEQ ID NO:744) of a native sequence PRO2564 cDNA, wherein SEQ ID NO:744 is a clone designated herein as "DNA83031".

40       Figure 745 shows the amino acid sequence (SEQ ID NO:745) derived from the coding sequence of SEQ ID NO:744 shown in Figure 744A-B.

Figure 746 shows a nucleotide sequence (SEQ ID NO:746) of a native sequence PRO83683 cDNA, wherein SEQ ID NO:746 is a clone designated herein as "DNA327700".

Figure 747 shows the amino acid sequence (SEQ ID NO:747) derived from the coding sequence of SEQ ID NO:746 shown in Figure 746.

5        Figure 748 shows a nucleotide sequence (SEQ ID NO:748) of a native sequence PRO82667 cDNA, wherein SEQ ID NO:748 is a clone designated herein as "DNA327701".

Figure 749 shows the amino acid sequence (SEQ ID NO:749) derived from the coding sequence of SEQ ID NO:748 shown in Figure 748.

10       Figure 750 shows a nucleotide sequence (SEQ ID NO:750) of a native sequence PRO83684 cDNA, wherein SEQ ID NO:750 is a clone designated herein as "DNA327702".

Figure 751 shows the amino acid sequence (SEQ ID NO:751) derived from the coding sequence of SEQ ID NO:750 shown in Figure 750.

Figure 752 shows a nucleotide sequence (SEQ ID NO:752) of a native sequence PRO83685 cDNA, wherein SEQ ID NO:752 is a clone designated herein as "DNA327703".

15       Figure 753 shows the amino acid sequence (SEQ ID NO:753) derived from the coding sequence of SEQ ID NO:752 shown in Figure 752.

Figure 754 shows a nucleotide sequence (SEQ ID NO:754) of a native sequence PRO58048 cDNA, wherein SEQ ID NO:754 is a clone designated herein as "DNA269636".

20       Figure 755 shows the amino acid sequence (SEQ ID NO:755) derived from the coding sequence of SEQ ID NO:754 shown in Figure 754.

Figure 756A-B shows a nucleotide sequence (SEQ ID NO:756) of a native sequence PRO81999 cDNA, wherein SEQ ID NO:756 is a clone designated herein as "DNA325478".

Figure 757 shows the amino acid sequence (SEQ ID NO:757) derived from the coding sequence of SEQ ID NO:756 shown in Figure 756A-B.

25       Figure 758 shows a nucleotide sequence (SEQ ID NO:758) of a native sequence PRO83686 cDNA, wherein SEQ ID NO:758 is a clone designated herein as "DNA327704".

Figure 759 shows the amino acid sequence (SEQ ID NO:759) derived from the coding sequence of SEQ ID NO:758 shown in Figure 758.

30       Figure 760 shows a nucleotide sequence (SEQ ID NO:760) of a native sequence PRO83687 cDNA, wherein SEQ ID NO:760 is a clone designated herein as "DNA327705".

Figure 761 shows the amino acid sequence (SEQ ID NO:761) derived from the coding sequence of SEQ ID NO:760 shown in Figure 760.

Figure 762 shows a nucleotide sequence (SEQ ID NO:762) of a native sequence PRO83688 cDNA, wherein SEQ ID NO:762 is a clone designated herein as "DNA327706".

35       Figure 763 shows the amino acid sequence (SEQ ID NO:763) derived from the coding sequence of SEQ ID NO:762 shown in Figure 762.

Figure 764 shows a nucleotide sequence (SEQ ID NO:764) of a native sequence PRO37752 cDNA, wherein SEQ ID NO:764 is a clone designated herein as "DNA227289".

40       Figure 765 shows the amino acid sequence (SEQ ID NO:765) derived from the coding sequence of SEQ ID NO:764 shown in Figure 764.

Figure 766 shows a nucleotide sequence (SEQ ID NO:766) of a native sequence PRO83689 cDNA, wherein SEQ ID NO:766 is a clone designated herein as "DNA327707".

Figure 767 shows the amino acid sequence (SEQ ID NO:767) derived from the coding sequence of SEQ ID NO:766 shown in Figure 766.

5        Figure 768 shows a nucleotide sequence (SEQ ID NO:768) of a native sequence cDNA, wherein SEQ ID NO:768 is a clone designated herein as "DNA327708".

Figure 769 shows a nucleotide sequence (SEQ ID NO:769) of a native sequence PRO21716 cDNA, wherein SEQ ID NO:769 is a clone designated herein as "DNA188204".

10       Figure 770 shows the amino acid sequence (SEQ ID NO:770) derived from the coding sequence of SEQ ID NO:769 shown in Figure 769.

Figure 771 shows a nucleotide sequence (SEQ ID NO:771) of a native sequence PRO83690 cDNA, wherein SEQ ID NO:771 is a clone designated herein as "DNA327709".

Figure 772 shows the amino acid sequence (SEQ ID NO:772) derived from the coding sequence of SEQ ID NO:771 shown in Figure 771.

15       Figure 773 shows a nucleotide sequence (SEQ ID NO:773) of a native sequence PRO81730 cDNA, wherein SEQ ID NO:773 is a clone designated herein as "DNA325163".

Figure 774 shows the amino acid sequence (SEQ ID NO:774) derived from the coding sequence of SEQ ID NO:773 shown in Figure 773.

20       Figure 775 shows a nucleotide sequence (SEQ ID NO:775) of a native sequence PRO83691 cDNA, wherein SEQ ID NO:775 is a clone designated herein as "DNA327710".

Figure 776 shows the amino acid sequence (SEQ ID NO:776) derived from the coding sequence of ~~SEQ ID NO:775 shown in Figure 775.~~

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Figure 777 shows a nucleotide sequence (SEQ ID NO:777) of a native sequence PRO83692 cDNA, wherein SEQ ID NO:777 is a clone designated herein as "DNA327711".

25       Figure 778 shows the amino acid sequence (SEQ ID NO:778) derived from the coding sequence of SEQ ID NO:777 shown in Figure 777.

Figure 779 shows a nucleotide sequence (SEQ ID NO:779) of a native sequence PRO11113 cDNA, wherein SEQ ID NO:779 is a clone designated herein as "DNA327712".

30       Figure 780 shows the amino acid sequence (SEQ ID NO:780) derived from the coding sequence of SEQ ID NO:779 shown in Figure 779.

Figure 781 shows a nucleotide sequence (SEQ ID NO:781) of a native sequence PRO37975 cDNA, wherein SEQ ID NO:781 is a clone designated herein as "DNA327713".

Figure 782 shows the amino acid sequence (SEQ ID NO:782) derived from the coding sequence of SEQ ID NO:781 shown in Figure 781.

35       Figure 783 shows a nucleotide sequence (SEQ ID NO:783) of a native sequence PRO81832 cDNA, wherein SEQ ID NO:783 is a clone designated herein as "DNA325285".

Figure 784 shows the amino acid sequence (SEQ ID NO:784) derived from the coding sequence of SEQ ID NO:783 shown in Figure .

40       Figure 785A-B shows a nucleotide sequence (SEQ ID NO:785) of a native sequence PRO83693 cDNA, wherein SEQ ID NO:785 is a clone designated herein as "DNA327714".

Figure 786 shows the amino acid sequence (SEQ ID NO:786) derived from the coding sequence of SEQ ID NO:785 shown in Figure 785.

Figure 787 shows a nucleotide sequence (SEQ ID NO:787) of a native sequence PRO83694 cDNA, wherein SEQ ID NO:787 is a clone designated herein as "DNA327715".

5        Figure 788 shows the amino acid sequence (SEQ ID NO:788) derived from the coding sequence of SEQ ID NO:787 shown in Figure 787.

Figure 789 shows a nucleotide sequence (SEQ ID NO:789) of a native sequence PRO82674 cDNA, wherein SEQ ID NO:789 is a clone designated herein as "DNA326267".

10       Figure 790 shows the amino acid sequence (SEQ ID NO:790) derived from the coding sequence of SEQ ID NO:789 shown in Figure 789.

Figure 791 shows a nucleotide sequence (SEQ ID NO:791) of a native sequence PRO4766 cDNA, wherein SEQ ID NO:791 is a clone designated herein as "DNA103439".

Figure 792 shows the amino acid sequence (SEQ ID NO:792) derived from the coding sequence of SEQ ID NO:791 shown in Figure 791.

15       Figure 793 shows a nucleotide sequence (SEQ ID NO:793) of a native sequence PRO37946 cDNA, wherein SEQ ID NO:793 is a clone designated herein as "DNA227483".

Figure 794 shows the amino acid sequence (SEQ ID NO:794) derived from the coding sequence of SEQ ID NO:793 shown in Figure 793.

20       Figure 795 shows a nucleotide sequence (SEQ ID NO:795) of a native sequence PRO61496 cDNA, wherein SEQ ID NO:795 is a clone designated herein as "DNA273515".

Figure 796 shows the amino acid sequence (SEQ ID NO:796) derived from the coding sequence of SEQ ID NO:795 shown in Figure 795.

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Figure 797 shows a nucleotide sequence (SEQ ID NO:797) of a native sequence PRO83695 cDNA, wherein SEQ ID NO:797 is a clone designated herein as "DNA327716".

25       Figure 798 shows the amino acid sequence (SEQ ID NO:798) derived from the coding sequence of SEQ ID NO:797 shown in Figure 797.

Figure 799 shows a nucleotide sequence (SEQ ID NO:799) of a native sequence PRO62702 cDNA, wherein SEQ ID NO:799 is a clone designated herein as "DNA274969".

30       Figure 800 shows the amino acid sequence (SEQ ID NO:800) derived from the coding sequence of SEQ ID NO:799 shown in Figure 799.

Figure 801 shows a nucleotide sequence (SEQ ID NO:801) of a native sequence PRO83696 cDNA, wherein SEQ ID NO:801 is a clone designated herein as "DNA327717".

Figure 802 shows the amino acid sequence (SEQ ID NO:802) derived from the coding sequence of SEQ ID NO:801 shown in Figure 801.

35       Figure 803 shows a nucleotide sequence (SEQ ID NO:803) of a native sequence cDNA, wherein SEQ ID NO:803 is a clone designated herein as "DNA274406".

Figure 804 shows a nucleotide sequence (SEQ ID NO:804) of a native sequence PRO83697 cDNA, wherein SEQ ID NO:804 is a clone designated herein as "DNA327718".

40       Figure 805 shows the amino acid sequence (SEQ ID NO:805) derived from the coding sequence of SEQ ID NO:804 shown in Figure 804.

Figure 806 shows a nucleotide sequence (SEQ ID NO:806) of a native sequence PRO58042 cDNA, wherein SEQ ID NO:806 is a clone designated herein as "DNA269630".

Figure 807 shows the amino acid sequence (SEQ ID NO:807) derived from the coding sequence of SEQ ID NO:806 shown in Figure 806.

5        Figure 808 shows a nucleotide sequence (SEQ ID NO:808) of a native sequence PRO83698 cDNA, wherein SEQ ID NO:808 is a clone designated herein as "DNA327719".

Figure 809 shows the amino acid sequence (SEQ ID NO:809) derived from the coding sequence of SEQ ID NO:808 shown in Figure 808.

10       Figure 810 shows a nucleotide sequence (SEQ ID NO:810) of a native sequence PRO83699 cDNA, wherein SEQ ID NO:810 is a clone designated herein as "DNA327720".

Figure 811 shows the amino acid sequence (SEQ ID NO:811) derived from the coding sequence of SEQ ID NO:810 shown in Figure 810.

Figure 812 shows a nucleotide sequence (SEQ ID NO:812) of a native sequence PRO81429 cDNA, wherein SEQ ID NO:812 is a clone designated herein as "DNA324816".

15       Figure 813 shows the amino acid sequence (SEQ ID NO:813) derived from the coding sequence of SEQ ID NO:812 shown in Figure 812.

Figure 814 shows a nucleotide sequence (SEQ ID NO:814) of a native sequence PRO83700 cDNA, wherein SEQ ID NO:814 is a clone designated herein as "DNA327721".

20       Figure 815 shows the amino acid sequence (SEQ ID NO:815) derived from the coding sequence of SEQ ID NO:814 shown in Figure 814.

Figure 816 shows a nucleotide sequence (SEQ ID NO:816) of a native sequence PRO36415 cDNA, wherein SEQ ID NO:816 is a clone designated herein as "DNA225952".

Figure 817 shows the amino acid sequence (SEQ ID NO:817) derived from the coding sequence of SEQ ID NO:816 shown in Figure 816.

25       Figure 818 shows a nucleotide sequence (SEQ ID NO:818) of a native sequence PRO83701 cDNA, wherein SEQ ID NO:818 is a clone designated herein as "DNA327722".

Figure 819 shows the amino acid sequence (SEQ ID NO:819) derived from the coding sequence of SEQ ID NO:818 shown in Figure 818.

30       Figure 820 shows a nucleotide sequence (SEQ ID NO:820) of a native sequence PRO61971 cDNA, wherein SEQ ID NO:820 is a clone designated herein as "DNA274027".

Figure 821 shows the amino acid sequence (SEQ ID NO:821) derived from the coding sequence of SEQ ID NO:820 shown in Figure 820.

Figure 822 shows a nucleotide sequence (SEQ ID NO:822) of a native sequence PRO83702 cDNA, wherein SEQ ID NO:822 is a clone designated herein as "DNA327723".

35       Figure 823 shows the amino acid sequence (SEQ ID NO:823) derived from the coding sequence of SEQ ID NO:822 shown in Figure 822.

Figure 824 shows a nucleotide sequence (SEQ ID NO:824) of a native sequence cDNA, wherein SEQ ID NO:824 is a clone designated herein as "DNA327724".

40       Figure 825 shows a nucleotide sequence (SEQ ID NO:825) of a native sequence PRO59053 cDNA, wherein SEQ ID NO:825 is a clone designated herein as "DNA270689".

Figure 826 shows the amino acid sequence (SEQ ID NO:826) derived from the coding sequence of SEQ ID NO:825 shown in Figure 825.

Figure 827 shows a nucleotide sequence (SEQ ID NO:827) of a native sequence PRO83703 cDNA, wherein SEQ ID NO:827 is a clone designated herein as "DNA327725".

5        Figure 828 shows the amino acid sequence (SEQ ID NO:828) derived from the coding sequence of SEQ ID NO:827 shown in Figure 827.

Figure 829A-B shows a nucleotide sequence (SEQ ID NO:829) of a native sequence PRO83704 cDNA, wherein SEQ ID NO:829 is a clone designated herein as "DNA327726".

10       Figure 830 shows the amino acid sequence (SEQ ID NO:830) derived from the coding sequence of SEQ ID NO:829 shown in Figure 829A-B.

Figure 831 shows a nucleotide sequence (SEQ ID NO:831) of a native sequence PRO83705 cDNA, wherein SEQ ID NO:831 is a clone designated herein as "DNA327727".

Figure 832 shows the amino acid sequence (SEQ ID NO:832) derived from the coding sequence of SEQ ID NO:831 shown in Figure 831.

15       Figure 833 shows a nucleotide sequence (SEQ ID NO:833) of a native sequence PRO4348 cDNA, wherein SEQ ID NO:833 is a clone designated herein as "DNA327728".

Figure 834 shows the amino acid sequence (SEQ ID NO:834) derived from the coding sequence of SEQ ID NO:833 shown in Figure 833.

20       Figure 835 shows a nucleotide sequence (SEQ ID NO:835) of a native sequence PRO36908 cDNA, wherein SEQ ID NO:835 is a clone designated herein as "DNA226445".

Figure 836 shows the amino acid sequence (SEQ ID NO:836) derived from the coding sequence of ~~SEQ ID NO:835 shown in Figure 835.~~

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Figure 837 shows a nucleotide sequence (SEQ ID NO:837) of a native sequence PRO62893 cDNA, wherein SEQ ID NO:837 is a clone designated herein as "DNA275195".

25       Figure 838 shows the amino acid sequence (SEQ ID NO:838) derived from the coding sequence of SEQ ID NO:837 shown in Figure 837.

Figure 839 shows a nucleotide sequence (SEQ ID NO:839) of a native sequence PRO58354 cDNA, wherein SEQ ID NO:839 is a clone designated herein as "DNA327729".

30       Figure 840 shows the amino acid sequence (SEQ ID NO:840) derived from the coding sequence of SEQ ID NO:839 shown in Figure 839.

Figure 841 shows a nucleotide sequence (SEQ ID NO:841) of a native sequence PRO83706 cDNA, wherein SEQ ID NO:841 is a clone designated herein as "DNA327730".

Figure 842 shows the amino acid sequence (SEQ ID NO:842) derived from the coding sequence of SEQ ID NO:841 shown in Figure 841.

35       Figure 843 shows a nucleotide sequence (SEQ ID NO:843) of a native sequence PRO83707 cDNA, wherein SEQ ID NO:843 is a clone designated herein as "DNA327731".

Figure 844 shows the amino acid sequence (SEQ ID NO:844) derived from the coding sequence of SEQ ID NO:843 shown in Figure 843.

40       Figure 845 shows a nucleotide sequence (SEQ ID NO:845) of a native sequence PRO61801 cDNA, wherein SEQ ID NO:845 is a clone designated herein as "DNA327732".



Figure 846 shows the amino acid sequence (SEQ ID NO:846) derived from the coding sequence of SEQ ID NO:845 shown in Figure 845.

Figure 847A-B shows a nucleotide sequence (SEQ ID NO:847) of a native sequence PRO83708 cDNA, wherein SEQ ID NO:847 is a clone designated herein as "DNA327733".

5        Figure 848 shows the amino acid sequence (SEQ ID NO:848) derived from the coding sequence of SEQ ID NO:847 shown in Figure 847.

Figure 849 shows a nucleotide sequence (SEQ ID NO:849) of a native sequence PRO83709 cDNA, wherein SEQ ID NO:849 is a clone designated herein as "DNA327734".

10       Figure 850 shows the amino acid sequence (SEQ ID NO:850) derived from the coding sequence of SEQ ID NO:849 shown in Figure 849.

Figure 851 shows a nucleotide sequence (SEQ ID NO:851) of a native sequence PRO83710 cDNA, wherein SEQ ID NO:851 is a clone designated herein as "DNA327735".

Figure 852 shows the amino acid sequence (SEQ ID NO:852) derived from the coding sequence of SEQ ID NO:851 shown in Figure 851.

15       Figure 853 shows a nucleotide sequence (SEQ ID NO:853) of a native sequence PRO70858 cDNA, wherein SEQ ID NO:853 is a clone designated herein as "DNA299884".

Figure 854 shows the amino acid sequence (SEQ ID NO:854) derived from the coding sequence of SEQ ID NO:853 shown in Figure 853.

20       Figure 855 shows a nucleotide sequence (SEQ ID NO:855) of a native sequence PRO2601 cDNA, wherein SEQ ID NO:855 is a clone designated herein as "DNA83128".

Figure 856 shows the amino acid sequence (SEQ ID NO:856) derived from the coding sequence of SEQ ID NO:855 shown in Figure 855.

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Figure 857 shows a nucleotide sequence (SEQ ID NO:857) of a native sequence PRO83711 cDNA, wherein SEQ ID NO:857 is a clone designated herein as "DNA327736".

25       Figure 858 shows the amino acid sequence (SEQ ID NO:858) derived from the coding sequence of SEQ ID NO:857 shown in Figure 857.

Figure 859 shows a nucleotide sequence (SEQ ID NO:859) of a native sequence PRO83712 cDNA, wherein SEQ ID NO:859 is a clone designated herein as "DNA327737".

30       Figure 860 shows the amino acid sequence (SEQ ID NO:860) derived from the coding sequence of SEQ ID NO:859 shown in Figure 859.

Figure 861 shows a nucleotide sequence (SEQ ID NO:861) of a native sequence PRO83713 cDNA, wherein SEQ ID NO:861 is a clone designated herein as "DNA327738".

Figure 862 shows the amino acid sequence (SEQ ID NO:862) derived from the coding sequence of SEQ ID NO:861 shown in Figure 861.

35       Figure 863 shows a nucleotide sequence (SEQ ID NO:863) of a native sequence PRO83714 cDNA, wherein SEQ ID NO:863 is a clone designated herein as "DNA327739".

Figure 864 shows the amino acid sequence (SEQ ID NO:864) derived from the coding sequence of SEQ ID NO:863 shown in Figure 863.

40       Figure 865 shows a nucleotide sequence (SEQ ID NO:865) of a native sequence PRO1787 cDNA, wherein SEQ ID NO:865 is a clone designated herein as "DNA327740".

Figure 866 shows the amino acid sequence (SEQ ID NO:866) derived from the coding sequence of SEQ ID NO:865 shown in Figure 865.

Figure 867 shows a nucleotide sequence (SEQ ID NO:867) of a native sequence PRO83715 cDNA, wherein SEQ ID NO:867 is a clone designated herein as "DNA327741".

5        Figure 868 shows the amino acid sequence (SEQ ID NO:868) derived from the coding sequence of SEQ ID NO:867 shown in Figure 867.

Figure 869 shows a nucleotide sequence (SEQ ID NO:869) of a native sequence PRO58969 cDNA, wherein SEQ ID NO:869 is a clone designated herein as "DNA270597".

10       Figure 870 shows the amino acid sequence (SEQ ID NO:870) derived from the coding sequence of SEQ ID NO:869 shown in Figure 869.

Figure 871A-D shows a nucleotide sequence (SEQ ID NO:871) of a native sequence PRO83716 cDNA, wherein SEQ ID NO:871 is a clone designated herein as "DNA327742".

Figure 872A-B shows the amino acid sequence (SEQ ID NO:872) derived from the coding sequence of SEQ ID NO:871 shown in Figure 871A-D.

15       Figure 873 shows a nucleotide sequence (SEQ ID NO:873) of a native sequence PRO83717 cDNA, wherein SEQ ID NO:873 is a clone designated herein as "DNA327743".

Figure 874 shows the amino acid sequence (SEQ ID NO:874) derived from the coding sequence of SEQ ID NO:873 shown in Figure 873.

20       Figure 875 shows a nucleotide sequence (SEQ ID NO:875) of a native sequence PRO60945 cDNA, wherein SEQ ID NO:875 is a clone designated herein as "DNA326821".

Figure 876 shows the amino acid sequence (SEQ ID NO:876) derived from the coding sequence of SEQ ID NO:875 shown in Figure 875.

Figure 877 shows a nucleotide sequence (SEQ ID NO:877) of a native sequence PRO71063 cDNA, wherein SEQ ID NO:877 is a clone designated herein as "DNA304499".

25       Figure 878 shows the amino acid sequence (SEQ ID NO:878) derived from the coding sequence of SEQ ID NO:877 shown in Figure 877.

Figure 879 shows a nucleotide sequence (SEQ ID NO:879) of a native sequence PRO83718 cDNA, wherein SEQ ID NO:879 is a clone designated herein as "DNA327744".

30       Figure 880 shows the amino acid sequence (SEQ ID NO:880) derived from the coding sequence of SEQ ID NO:879 shown in Figure 879.

Figure 881 shows a nucleotide sequence (SEQ ID NO:881) of a native sequence PRO83719 cDNA, wherein SEQ ID NO:881 is a clone designated herein as "DNA327745".

Figure 882 shows the amino acid sequence (SEQ ID NO:882) derived from the coding sequence of SEQ ID NO:881 shown in Figure 881.

35       Figure 883 shows a nucleotide sequence (SEQ ID NO:883) of a native sequence PRO83720 cDNA, wherein SEQ ID NO:883 is a clone designated herein as "DNA327746".

Figure 884 shows the amino acid sequence (SEQ ID NO:884) derived from the coding sequence of SEQ ID NO:883 shown in Figure 883.

40       Figure 885 shows a nucleotide sequence (SEQ ID NO:885) of a native sequence PRO25204 cDNA, wherein SEQ ID NO:885 is a clone designated herein as "DNA196754".

Figure 886 shows the amino acid sequence (SEQ ID NO:886) derived from the coding sequence of SEQ ID NO:885 shown in Figure 885.

Figure 887 shows a nucleotide sequence (SEQ ID NO:887) of a native sequence PRO60397 cDNA, wherein SEQ ID NO:887 is a clone designated herein as "DNA272127".

5        Figure 888 shows the amino acid sequence (SEQ ID NO:888) derived from the coding sequence of SEQ ID NO:887 shown in Figure 887.

Figure 889 shows a nucleotide sequence (SEQ ID NO:889) of a native sequence PRO83721 cDNA, wherein SEQ ID NO:889 is a clone designated herein as "DNA327747".

10       Figure 890 shows the amino acid sequence (SEQ ID NO:890) derived from the coding sequence of SEQ ID NO:889 shown in Figure 889.

Figure 891 shows a nucleotide sequence (SEQ ID NO:891) of a native sequence PRO4575 cDNA, wherein SEQ ID NO:891 is a clone designated herein as "DNA103245".

Figure 892 shows the amino acid sequence (SEQ ID NO:892) derived from the coding sequence of SEQ ID NO:891 shown in Figure 891.

15       Figure 893 shows a nucleotide sequence (SEQ ID NO:893) of a native sequence PRO37550 cDNA, wherein SEQ ID NO:893 is a clone designated herein as "DNA227087".

Figure 894 shows the amino acid sequence (SEQ ID NO:894) derived from the coding sequence of SEQ ID NO:893 shown in Figure 893.

20       Figure 895 shows a nucleotide sequence (SEQ ID NO:895) of a native sequence PRO36541 cDNA, wherein SEQ ID NO:895 is a clone designated herein as "DNA226078".

Figure 896 shows the amino acid sequence (SEQ ID NO:896) derived from the coding sequence of SEQ ID NO:895 shown in Figure 895.

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Figure 897A-B shows a nucleotide sequence (SEQ ID NO:897) of a native sequence PRO2537 cDNA, wherein SEQ ID NO:897 is a clone designated herein as "DNA76504".

25       Figure 898 shows the amino acid sequence (SEQ ID NO:898) derived from the coding sequence of SEQ ID NO:897 shown in Figure 897A-B.

Figure 899 shows a nucleotide sequence (SEQ ID NO:899) of a native sequence PRO83722 cDNA, wherein SEQ ID NO:899 is a clone designated herein as "DNA327748".

30       Figure 900 shows the amino acid sequence (SEQ ID NO:900) derived from the coding sequence of SEQ ID NO:899 shown in Figure 899.

Figure 901 shows a nucleotide sequence (SEQ ID NO:901) of a native sequence PRO83723 cDNA, wherein SEQ ID NO:901 is a clone designated herein as "DNA327749".

Figure 902 shows the amino acid sequence (SEQ ID NO:902) derived from the coding sequence of SEQ ID NO:901 shown in Figure 901.

35       Figure 903 shows a nucleotide sequence (SEQ ID NO:903) of a native sequence PRO83724 cDNA, wherein SEQ ID NO:903 is a clone designated herein as "DNA327750".

Figure 904 shows the amino acid sequence (SEQ ID NO:904) derived from the coding sequence of SEQ ID NO:903 shown in Figure 903.

40       Figure 905 shows a nucleotide sequence (SEQ ID NO:905) of a native sequence PRO61480 cDNA, wherein SEQ ID NO:905 is a clone designated herein as "DNA327751".

Figure 906 shows the amino acid sequence (SEQ ID NO:906) derived from the coding sequence of SEQ ID NO:905 shown in Figure 905.

Figure 907 shows a nucleotide sequence (SEQ ID NO:907) of a native sequence PRO2695 cDNA, wherein SEQ ID NO:907 is a clone designated herein as "DNA88198".

5        Figure 908 shows the amino acid sequence (SEQ ID NO:908) derived from the coding sequence of SEQ ID NO:907 shown in Figure 907.

Figure 909 shows a nucleotide sequence (SEQ ID NO:909) of a native sequence cDNA, wherein SEQ ID NO:909 is a clone designated herein as "DNA327752".

10       Figure 910 shows a nucleotide sequence (SEQ ID NO:910) of a native sequence PRO20144 cDNA, wherein SEQ ID NO:910 is a clone designated herein as "DNA171416".

Figure 911 shows the amino acid sequence (SEQ ID NO:911) derived from the coding sequence of SEQ ID NO:910 shown in Figure 910.

Figure 912 shows a nucleotide sequence (SEQ ID NO:912) of a native sequence PRO51365 cDNA, wherein SEQ ID NO:912 is a clone designated herein as "DNA327753".

15       Figure 913 shows the amino acid sequence (SEQ ID NO:913) derived from the coding sequence of SEQ ID NO:912 shown in Figure 912.

Figure 914 shows a nucleotide sequence (SEQ ID NO:914) of a native sequence PRO4526 cDNA, wherein SEQ ID NO:914 is a clone designated herein as "DNA327754".

20       Figure 915 shows the amino acid sequence (SEQ ID NO:915) derived from the coding sequence of SEQ ID NO:914 shown in Figure 914.

Figure 916 shows a nucleotide sequence (SEQ ID NO:916) of a native sequence PRO83725 cDNA, wherein SEQ ID NO:916 is a clone designated herein as "DNA327755".

Figure 917 shows the amino acid sequence (SEQ ID NO:917) derived from the coding sequence of SEQ ID NO:916 shown in Figure 916.

25       Figure 918 shows a nucleotide sequence (SEQ ID NO:918) of a native sequence PRO83726 cDNA, wherein SEQ ID NO:918 is a clone designated herein as "DNA327756".

Figure 919 shows the amino acid sequence (SEQ ID NO:919) derived from the coding sequence of SEQ ID NO:918 shown in Figure 918.

30       Figure 920A-B shows a nucleotide sequence (SEQ ID NO:920) of a native sequence PRO60082 cDNA, wherein SEQ ID NO:920 is a clone designated herein as "DNA327757".

Figure 921 shows the amino acid sequence (SEQ ID NO:921) derived from the coding sequence of SEQ ID NO:920 shown in Figure 920A-B.

Figure 922 shows a nucleotide sequence (SEQ ID NO:922) of a native sequence PRO81272 cDNA, wherein SEQ ID NO:922 is a clone designated herein as "DNA324626".

35       Figure 923 shows the amino acid sequence (SEQ ID NO:923) derived from the coding sequence of SEQ ID NO:922 shown in Figure 922.

Figure 924A-D shows a nucleotide sequence (SEQ ID NO:924) of a native sequence PRO83727 cDNA, wherein SEQ ID NO:924 is a clone designated herein as "DNA327758".

40       Figure 925 shows the amino acid sequence (SEQ ID NO:925) derived from the coding sequence of SEQ ID NO:924 shown in Figure 924A-D.

Figure 926 shows a nucleotide sequence (SEQ ID NO:926) of a native sequence PRO83728 cDNA, wherein SEQ ID NO:926 is a clone designated herein as "DNA327759".

Figure 927 shows the amino acid sequence (SEQ ID NO:927) derived from the coding sequence of SEQ ID NO:926 shown in Figure 926.

5        Figure 928 shows a nucleotide sequence (SEQ ID NO:928) of a native sequence PRO59647 cDNA, wherein SEQ ID NO:928 is a clone designated herein as "DNA271344".

Figure 929 shows the amino acid sequence (SEQ ID NO:929) derived from the coding sequence of SEQ ID NO:928 shown in Figure 928.

10       Figure 930 shows a nucleotide sequence (SEQ ID NO:930) of a native sequence PRO80955 cDNA, wherein SEQ ID NO:930 is a clone designated herein as "DNA324272".

Figure 931 shows the amino acid sequence (SEQ ID NO:931) derived from the coding sequence of SEQ ID NO:930 shown in Figure 930.

Figure 932 shows a nucleotide sequence (SEQ ID NO:932) of a native sequence PRO21787 cDNA, wherein SEQ ID NO:932 is a clone designated herein as "DNA188293".

15       Figure 933 shows the amino acid sequence (SEQ ID NO:933) derived from the coding sequence of SEQ ID NO:932 shown in Figure 932.

Figure 934 shows a nucleotide sequence (SEQ ID NO:934) of a native sequence PRO83729 cDNA, wherein SEQ ID NO:934 is a clone designated herein as "DNA327760".

20       Figure 935 shows the amino acid sequence (SEQ ID NO:935) derived from the coding sequence of SEQ ID NO:934 shown in Figure 934.

Figure 936 shows a nucleotide sequence (SEQ ID NO:936) of a native sequence PRO83730 cDNA, wherein ~~SEQ ID NO:936 is a clone designated herein as "DNA327761".~~

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Figure 937 shows the amino acid sequence (SEQ ID NO:937) derived from the coding sequence of SEQ ID NO:936 shown in Figure 936.

25       Figure 938 shows a nucleotide sequence (SEQ ID NO:938) of a native sequence cDNA, wherein SEQ ID NO:938 is a clone designated herein as "DNA327762".

Figure 939 shows a nucleotide sequence (SEQ ID NO:939) of a native sequence PRO83731 cDNA, wherein SEQ ID NO:939 is a clone designated herein as "DNA327763".

30       Figure 940 shows the amino acid sequence (SEQ ID NO:940) derived from the coding sequence of SEQ ID NO:939 shown in Figure 939.

Figure 941 shows a nucleotide sequence (SEQ ID NO:941) of a native sequence cDNA, wherein SEQ ID NO:941 is a clone designated herein as "DNA327764".

Figure 942A-C shows a nucleotide sequence (SEQ ID NO:942) of a native sequence PRO83732 cDNA, wherein SEQ ID NO:942 is a clone designated herein as "DNA327765".

35       Figure 943 shows the amino acid sequence (SEQ ID NO:943) derived from the coding sequence of SEQ ID NO:942 shown in Figure 942A-C.

Figure 944A-B shows a nucleotide sequence (SEQ ID NO:944) of a native sequence cDNA, wherein SEQ ID NO:944 is a clone designated herein as "DNA194332".

40       Figure 945 shows a nucleotide sequence (SEQ ID NO:945) of a native sequence PRO69690 cDNA, wherein SEQ ID NO:945 is a clone designated herein as "DNA287433".

Figure 946 shows the amino acid sequence (SEQ ID NO:946) derived from the coding sequence of SEQ ID NO:945 shown in Figure 945.

Figure 947 shows a nucleotide sequence (SEQ ID NO:947) of a native sequence PRO83733 cDNA, wherein SEQ ID NO:947 is a clone designated herein as "DNA327766".

5        Figure 948 shows the amino acid sequence (SEQ ID NO:948) derived from the coding sequence of SEQ ID NO:947 shown in Figure 947.

Figure 949A-B shows a nucleotide sequence (SEQ ID NO:949) of a native sequence PRO83734 cDNA, wherein SEQ ID NO:949 is a clone designated herein as "DNA327767".

10       Figure 950 shows the amino acid sequence (SEQ ID NO:950) derived from the coding sequence of SEQ ID NO:949 shown in Figure 949A-B.

Figure 951 shows a nucleotide sequence (SEQ ID NO:951) of a native sequence PRO119 cDNA, wherein SEQ ID NO:951 is a clone designated herein as "DNA52750".

Figure 952 shows the amino acid sequence (SEQ ID NO:952) derived from the coding sequence of SEQ ID NO:951 shown in Figure 951.

15       Figure 953 shows a nucleotide sequence (SEQ ID NO:953) of a native sequence cDNA, wherein SEQ ID NO:953 is a clone designated herein as "DNA327768".

Figure 954 shows a nucleotide sequence (SEQ ID NO:954) of a native sequence PRO83735 cDNA, wherein SEQ ID NO:954 is a clone designated herein as "DNA327769".

20       Figure 955 shows the amino acid sequence (SEQ ID NO:955) derived from the coding sequence of SEQ ID NO:954 shown in Figure 954.

Figure 956 shows a nucleotide sequence (SEQ ID NO:956) of a native sequence PRO83736 cDNA, wherein SEQ ID NO:956 is a clone designated herein as "DNA327770".

Figure 957 shows the amino acid sequence (SEQ ID NO:957) derived from the coding sequence of SEQ ID NO:956 shown in Figure 956.

25       Figure 958 shows a nucleotide sequence (SEQ ID NO:958) of a native sequence PRO12179 cDNA, wherein SEQ ID NO:958 is a clone designated herein as "DNA151120".

Figure 959 shows the amino acid sequence (SEQ ID NO:959) derived from the coding sequence of SEQ ID NO:958 shown in Figure 958.

30       Figure 960 shows a nucleotide sequence (SEQ ID NO:960) of a native sequence PRO83737 cDNA, wherein SEQ ID NO:960 is a clone designated herein as "DNA327771".

Figure 961 shows the amino acid sequence (SEQ ID NO:961) derived from the coding sequence of SEQ ID NO:960 shown in Figure 960.

Figure 962A-B shows a nucleotide sequence (SEQ ID NO:962) of a native sequence cDNA, wherein SEQ ID NO:962 is a clone designated herein as "DNA228024".

35       Figure 963 shows a nucleotide sequence (SEQ ID NO:963) of a native sequence cDNA, wherein SEQ ID NO:963 is a clone designated herein as "DNA150980".

Figure 964 shows a nucleotide sequence (SEQ ID NO:964) of a native sequence cDNA, wherein SEQ ID NO:964 is a clone designated herein as "DNA327772".

40       Figure 965A-B shows a nucleotide sequence (SEQ ID NO:965) of a native sequence PRO83739 cDNA, wherein SEQ ID NO:965 is a clone designated herein as "DNA327773".

Figure 966 shows the amino acid sequence (SEQ ID NO:966) derived from the coding sequence of SEQ ID NO:965 shown in Figure 965.

Figure 967 shows a nucleotide sequence (SEQ ID NO:967) of a native sequence PRO83740 cDNA, wherein SEQ ID NO:967 is a clone designated herein as "DNA327774".

5 Figure 968 shows the amino acid sequence (SEQ ID NO:968) derived from the coding sequence of SEQ ID NO:967 shown in Figure 967.

Figure 969A-C shows a nucleotide sequence (SEQ ID NO:969) of a native sequence PRO83741 cDNA, wherein SEQ ID NO:969 is a clone designated herein as "DNA327775".

10 Figure 970 shows the amino acid sequence (SEQ ID NO:970) derived from the coding sequence of SEQ ID NO:969 shown in Figure 969A-C.

Figure 971A-B shows a nucleotide sequence (SEQ ID NO:971) of a native sequence PRO49304 cDNA, wherein SEQ ID NO:971 is a clone designated herein as "DNA254192".

Figure 972 shows the amino acid sequence (SEQ ID NO:972) derived from the coding sequence of SEQ ID NO:971 shown in Figure 971A-B.

15 Figure 973A-B shows a nucleotide sequence (SEQ ID NO:973) of a native sequence PRO62241 cDNA, wherein SEQ ID NO:973 is a clone designated herein as "DNA274322".

Figure 974 shows the amino acid sequence (SEQ ID NO:974) derived from the coding sequence of SEQ ID NO:973 shown in Figure 973A-B.

20 Figure 975 shows a nucleotide sequence (SEQ ID NO:975) of a native sequence PRO36504 cDNA, wherein SEQ ID NO:975 is a clone designated herein as "DNA226041".

Figure 976 shows the amino acid sequence (SEQ ID NO:976) derived from the coding sequence of SEQ ID NO:975 shown in Figure 975.

Figure 977 shows a nucleotide sequence (SEQ ID NO:977) of a native sequence PRO83742 cDNA, wherein SEQ ID NO:977 is a clone designated herein as "DNA327776".

25 Figure 978 shows the amino acid sequence (SEQ ID NO:978) derived from the coding sequence of SEQ ID NO:977 shown in Figure 977.

Figure 979 shows a nucleotide sequence (SEQ ID NO:979) of a native sequence PRO11833 cDNA, wherein SEQ ID NO:979 is a clone designated herein as "DNA151487".

30 Figure 980 shows the amino acid sequence (SEQ ID NO:980) derived from the coding sequence of SEQ ID NO:979 shown in Figure 979.

Figure 981A-D shows a nucleotide sequence (SEQ ID NO:981) of a native sequence cDNA, wherein SEQ ID NO:981 is a clone designated herein as "DNA327777".

Figure 982A-B shows a nucleotide sequence (SEQ ID NO:982) of a native sequence cDNA, wherein SEQ ID NO:982 is a clone designated herein as "DNA327778".

35 Figure 983A-B shows a nucleotide sequence (SEQ ID NO:983) of a native sequence cDNA, wherein SEQ ID NO:983 is a clone designated herein as "DNA270118".

Figure 984A-B shows a nucleotide sequence (SEQ ID NO:984) of a native sequence PRO83744 cDNA, wherein SEQ ID NO:984 is a clone designated herein as "DNA327779".

40 Figure 985 shows the amino acid sequence (SEQ ID NO:985) derived from the coding sequence of SEQ ID NO:984 shown in Figure 984A-B.

Figure 986A-B shows a nucleotide sequence (SEQ ID NO:986) of a native sequence cDNA, wherein SEQ ID NO:986 is a clone designated herein as "DNA327780".

Figure 987A-B shows a nucleotide sequence (SEQ ID NO:987) of a native sequence PRO83745 cDNA, wherein SEQ ID NO:987 is a clone designated herein as "DNA327781".

5        Figure 988 shows the amino acid sequence (SEQ ID NO:988) derived from the coding sequence of SEQ ID NO:987 shown in Figure 987A-B.

Figure 989 shows a nucleotide sequence (SEQ ID NO:989) of a native sequence cDNA, wherein SEQ ID NO:989 is a clone designated herein as "DNA327782".

10       Figure 990 shows a nucleotide sequence (SEQ ID NO:990) of a native sequence PRO83747 cDNA, wherein SEQ ID NO:990 is a clone designated herein as "DNA327783".

Figure 991 shows the amino acid sequence (SEQ ID NO:991) derived from the coding sequence of SEQ ID NO:990 shown in Figure 990.

Figure 992A-B shows a nucleotide sequence (SEQ ID NO:992) of a native sequence PRO83748 cDNA, wherein SEQ ID NO:992 is a clone designated herein as "DNA327784".

15       Figure 993 shows the amino acid sequence (SEQ ID NO:993) derived from the coding sequence of SEQ ID NO:992 shown in Figure 992A-B.

Figure 994 shows a nucleotide sequence (SEQ ID NO:994) of a native sequence PRO80622 cDNA, wherein SEQ ID NO:994 is a clone designated herein as "DNA323879".

20       Figure 995 shows the amino acid sequence (SEQ ID NO:995) derived from the coding sequence of SEQ ID NO:994 shown in Figure 994.

Figure 996 shows a nucleotide sequence (SEQ ID NO:996) of a native sequence PRO83749 cDNA, wherein SEQ ID NO:996 is a clone designated herein as "DNA327785".

Figure 997 shows the amino acid sequence (SEQ ID NO:997) derived from the coding sequence of SEQ ID NO:996 shown in Figure 996.

25       Figure 998 shows a nucleotide sequence (SEQ ID NO:998) of a native sequence cDNA, wherein SEQ ID NO:998 is a clone designated herein as "DNA327786".

Figure 999 shows a nucleotide sequence (SEQ ID NO:999) of a native sequence PRO83751 cDNA, wherein SEQ ID NO:999 is a clone designated herein as "DNA327787".

30       Figure 1000 shows the amino acid sequence (SEQ ID NO:1000) derived from the coding sequence of SEQ ID NO:999 shown in Figure 999.

Figure 1001 shows a nucleotide sequence (SEQ ID NO:1001) of a native sequence PRO83752 cDNA, wherein SEQ ID NO:1001 is a clone designated herein as "DNA327788".

Figure 1002 shows the amino acid sequence (SEQ ID NO:1002) derived from the coding sequence of SEQ ID NO:1001 shown in Figure 1001.

35       Figure 1003 shows a nucleotide sequence (SEQ ID NO:1003) of a native sequence cDNA, wherein SEQ ID NO:1003 is a clone designated herein as "DNA228053".

Figure 1004 shows a nucleotide sequence (SEQ ID NO:1004) of a native sequence PRO54720 cDNA, wherein SEQ ID NO:1004 is a clone designated herein as "DNA260974".

40       Figure 1005 shows the amino acid sequence (SEQ ID NO:1005) derived from the coding sequence of SEQ ID NO:1004 shown in Figure 1004.



Figure 1006A-B shows a nucleotide sequence (SEQ ID NO:1006) of a native sequence PRO50245 cDNA, wherein SEQ ID NO:1006 is a clone designated herein as "DNA255165".

Figure 1007 shows the amino acid sequence (SEQ ID NO:1007) derived from the coding sequence of SEQ ID NO:1006 shown in Figure 1006A-B.

5 Figure 1008 shows a nucleotide sequence (SEQ ID NO:1008) of a native sequence PRO83753 cDNA, wherein SEQ ID NO:1008 is a clone designated herein as "DNA327789".

Figure 1009 shows the amino acid sequence (SEQ ID NO:1009) derived from the coding sequence of SEQ ID NO:1008 shown in Figure 1008.

10 Figure 1010 shows a nucleotide sequence (SEQ ID NO:1010) of a native sequence PRO83754 cDNA, wherein SEQ ID NO:1010 is a clone designated herein as "DNA327790".

Figure 1011 shows the amino acid sequence (SEQ ID NO:1011) derived from the coding sequence of SEQ ID NO:1010 shown in Figure 1010.

Figure 1012A-B shows a nucleotide sequence (SEQ ID NO:1012) of a native sequence PRO83755 cDNA, wherein SEQ ID NO:1012 is a clone designated herein as "DNA327791".

15 Figure 1013 shows the amino acid sequence (SEQ ID NO:1013) derived from the coding sequence of SEQ ID NO:1012 shown in Figure 1012A-B.

Figure 1014A-B shows a nucleotide sequence (SEQ ID NO:1014) of a native sequence PRO 83756 cDNA, wherein SEQ ID NO: is a clone designated herein as "DNA327792".

20 Figure 1015 shows the amino acid sequence (SEQ ID NO:1015) derived from the coding sequence of SEQ ID NO:1014 shown in Figure 1014A-B.

Figure 1016 shows a nucleotide sequence (SEQ ID NO:1016) of a native sequence PRO83757 cDNA, wherein SEQ ID NO:1016 is a clone designated herein as "DNA327793".

Figure 1017 shows the amino acid sequence (SEQ ID NO:1017) derived from the coding sequence of SEQ ID NO:1016 shown in Figure 1016.

25 Figure 1018A-D shows a nucleotide sequence (SEQ ID NO:1018) of a native sequence PRO83758 cDNA, wherein SEQ ID NO:1018 is a clone designated herein as "DNA327794".

Figure 1019 shows the amino acid sequence (SEQ ID NO:1019) derived from the coding sequence of SEQ ID NO:1018 shown in Figure 1018A-D.

30 Figure 1020 shows a nucleotide sequence (SEQ ID NO:1020) of a native sequence cDNA, wherein SEQ ID NO:1020 is a clone designated herein as "DNA327795".

Figure 1021 shows a nucleotide sequence (SEQ ID NO:1021) of a native sequence PRO83760 cDNA, wherein SEQ ID NO:1021 is a clone designated herein as "DNA327796".

Figure 1022 shows the amino acid sequence (SEQ ID NO:1022) derived from the coding sequence of SEQ ID NO:1021 shown in Figure 1021.

35 Figure 1023 shows a nucleotide sequence (SEQ ID NO:1023) of a native sequence PRO83761 cDNA, wherein SEQ ID NO:1023 is a clone designated herein as "DNA327797".

Figure 1024 shows the amino acid sequence (SEQ ID NO:1024) derived from the coding sequence of SEQ ID NO:1023 shown in Figure 1023.

40 Figure 1025 shows a nucleotide sequence (SEQ ID NO:1025) of a native sequence PRO83762 cDNA, wherein SEQ ID NO:1025 is a clone designated herein as "DNA327798".

Figure 1026 shows the amino acid sequence (SEQ ID NO:1026) derived from the coding sequence of SEQ ID NO:1025 shown in Figure 1025.

Figure 1027 shows a nucleotide sequence (SEQ ID NO:1027) of a native sequence PRO40011 cDNA, wherein SEQ ID NO:1027 is a clone designated herein as "DNA327799".

5        Figure 1028 shows the amino acid sequence (SEQ ID NO:1028) derived from the coding sequence of SEQ ID NO:1027 shown in Figure 1027.

Figure 1029 shows a nucleotide sequence (SEQ ID NO:1029) of a native sequence PRO83763 cDNA, wherein SEQ ID NO:1029 is a clone designated herein as "DNA327800".

10       Figure 1030 shows the amino acid sequence (SEQ ID NO:1030) derived from the coding sequence of SEQ ID NO:1029 shown in Figure 1029.

Figure 1031 shows a nucleotide sequence (SEQ ID NO:1031) of a native sequence PRO11792 cDNA, wherein SEQ ID NO:1031 is a clone designated herein as "DNA151422".

Figure 1032 shows the amino acid sequence (SEQ ID NO:1032) derived from the coding sequence of SEQ ID NO:1031 shown in Figure 1031.

15       Figure 1033 shows a nucleotide sequence (SEQ ID NO:1033) of a native sequence PRO83764 cDNA, wherein SEQ ID NO:1033 is a clone designated herein as "DNA327801".

Figure 1034 shows the amino acid sequence (SEQ ID NO:1034) derived from the coding sequence of SEQ ID NO:1033 shown in Figure 1033.

20       Figure 1035 shows a nucleotide sequence (SEQ ID NO:1035) of a native sequence PRO71208 cDNA, wherein SEQ ID NO:1035 is a clone designated herein as "DNA304796".

Figure 1036 shows the amino acid sequence (SEQ ID NO:1036) derived from the coding sequence of SEQ ID NO:1035 shown in Figure 1035.

Figure 1037 shows a nucleotide sequence (SEQ ID NO:1037) of a native sequence PRO83765 cDNA, wherein SEQ ID NO:1037 is a clone designated herein as "DNA327802".

25       Figure 1038 shows the amino acid sequence (SEQ ID NO:1083) derived from the coding sequence of SEQ ID NO:1037 shown in Figure 1037.

Figure 1039A-B shows a nucleotide sequence (SEQ ID NO:1039) of a native sequence PRO83766 cDNA, wherein SEQ ID NO:1039 is a clone designated herein as "DNA327803".

30       Figure 1040 shows the amino acid sequence (SEQ ID NO:1040) derived from the coding sequence of SEQ ID NO:1039 shown in Figure 1039A-B.

Figure 1041 shows a nucleotide sequence (SEQ ID NO:1041) of a native sequence PRO61547 cDNA, wherein SEQ ID NO:1041 is a clone designated herein as "DNA273569".

Figure 1042 shows the amino acid sequence (SEQ ID NO:1042) derived from the coding sequence of SEQ ID NO:1041 shown in Figure 1041.

35       Figure 1043 shows a nucleotide sequence (SEQ ID NO:1043) of a native sequence PRO69493 cDNA, wherein SEQ ID NO:1043 is a clone designated herein as "DNA327804".

Figure 1044 shows the amino acid sequence (SEQ ID NO:1044) derived from the coding sequence of SEQ ID NO:1043 shown in Figure 1043.

40       Figure 1045 shows a nucleotide sequence (SEQ ID NO:1045) of a native sequence cDNA, wherein SEQ ID NO:1045 is a clone designated herein as "DNA327805".

Figure 1046 shows a nucleotide sequence (SEQ ID NO:1046) of a native sequence PRO83767 cDNA, wherein SEQ ID NO:1046 is a clone designated herein as "DNA327806".

Figure 1047 shows the amino acid sequence (SEQ ID NO:1047) derived from the coding sequence of SEQ ID NO:1046 shown in Figure 1046.

5        Figure 1048 shows a nucleotide sequence (SEQ ID NO:1048) of a native sequence PRO83768 cDNA, wherein SEQ ID NO:1048 is a clone designated herein as "DNA327807".

Figure 1049 shows the amino acid sequence (SEQ ID NO:1049) derived from the coding sequence of SEQ ID NO:1048 shown in Figure 1048.

10        Figure 1050 shows a nucleotide sequence (SEQ ID NO:1050) of a native sequence PRO83769 cDNA, wherein SEQ ID NO:1050 is a clone designated herein as "DNA327808".

Figure 1051 shows the amino acid sequence (SEQ ID NO:1051) derived from the coding sequence of SEQ ID NO:1050 shown in Figure 1050.

Figure 1052 shows a nucleotide sequence (SEQ ID NO:1052) of a native sequence PRO83770 cDNA, wherein SEQ ID NO:1052 is a clone designated herein as "DNA327809".

15        Figure 1053 shows the amino acid sequence (SEQ ID NO:1053) derived from the coding sequence of SEQ ID NO:1052 shown in Figure 1052.

Figure 1054A-C shows a nucleotide sequence (SEQ ID NO:1054) of a native sequence PRO12903 cDNA, wherein SEQ ID NO:1054 is a clone designated herein as "DNA151840".

20        Figure 1055 shows the amino acid sequence (SEQ ID NO:1055) derived from the coding sequence of SEQ ID NO:1054 shown in Figure 1054A-C.

Figure 1056 shows a nucleotide sequence (SEQ ID NO:1056) of a native sequence PRO83771 cDNA, wherein SEQ ID NO:1056 is a clone designated herein as "DNA327810".

Figure 1057 shows the amino acid sequence (SEQ ID NO:1057) derived from the coding sequence of SEQ ID NO:1056 shown in Figure 1056.

25        Figure 1058A-B shows a nucleotide sequence (SEQ ID NO:1058) of a native sequence cDNA, wherein SEQ ID NO:1058 is a clone designated herein as "DNA256455".

Figure 1059 shows a nucleotide sequence (SEQ ID NO:1059) of a native sequence PRO83772 cDNA, wherein SEQ ID NO:1059 is a clone designated herein as "DNA327811".

30        Figure 1060 shows the amino acid sequence (SEQ ID NO:1060) derived from the coding sequence of SEQ ID NO:1059 shown in Figure 1059.

Figure 1061 shows a nucleotide sequence (SEQ ID NO:1061) of a native sequence PRO49268 cDNA, wherein SEQ ID NO:1061 is a clone designated herein as "DNA254153".

Figure 1062 shows the amino acid sequence (SEQ ID NO:1062) derived from the coding sequence of SEQ ID NO:1061 shown in Figure 1061.

35        Figure 1063 shows a nucleotide sequence (SEQ ID NO:1063) of a native sequence PRO83773 cDNA, wherein SEQ ID NO:1063 is a clone designated herein as "DNA327812".

Figure 1064 shows the amino acid sequence (SEQ ID NO:1064) derived from the coding sequence of SEQ ID NO:1063 shown in Figure 1063.

40        Figure 1065 shows a nucleotide sequence (SEQ ID NO:1065) of a native sequence PRO83774 cDNA, wherein SEQ ID NO:1065 is a clone designated herein as "DNA327813".

Figure 1066 shows the amino acid sequence (SEQ ID NO:1066) derived from the coding sequence of SEQ ID NO:1065 shown in Figure 1065.

Figure 1067 shows a nucleotide sequence (SEQ ID NO:1067) of a native sequence PRO38184 cDNA, wherein SEQ ID NO:1067 is a clone designated herein as "DNA227721".

5        Figure 1068 shows the amino acid sequence (SEQ ID NO:1068) derived from the coding sequence of SEQ ID NO:1067 shown in Figure 1067.

Figure 1069 shows a nucleotide sequence (SEQ ID NO:1069) of a native sequence PRO71203 cDNA, wherein SEQ ID NO:1069 is a clone designated herein as "DNA304791".

10       Figure 1070 shows the amino acid sequence (SEQ ID NO:1070) derived from the coding sequence of SEQ ID NO:1069 shown in Figure 1069.

Figure 1071 shows a nucleotide sequence (SEQ ID NO:1071) of a native sequence PRO58654 cDNA, wherein SEQ ID NO:1071 is a clone designated herein as "DNA270266".

Figure 1072 shows the amino acid sequence (SEQ ID NO:1072) derived from the coding sequence of SEQ ID NO:1071 shown in Figure 1071.

15       Figure 1073 shows a nucleotide sequence (SEQ ID NO:1073) of a native sequence PRO2038 cDNA, wherein SEQ ID NO:1073 is a clone designated herein as "DNA327814".

Figure 1074 shows the amino acid sequence (SEQ ID NO:1074) derived from the coding sequence of SEQ ID NO:1073 shown in Figure 1073.

20       Figure 1075 shows a nucleotide sequence (SEQ ID NO:1075) of a native sequence PRO61547 cDNA, wherein SEQ ID NO:1075 is a clone designated herein as "DNA327815".

Figure 1076 shows the amino acid sequence (SEQ ID NO:1076) derived from the coding sequence of SEQ ID NO:1075 shown in Figure 1075.

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Figure 1077 shows a nucleotide sequence (SEQ ID NO:1077) of a native sequence PRO82146 cDNA, wherein SEQ ID NO:1077 is a clone designated herein as "DNA327816".

25       Figure 1078 shows the amino acid sequence (SEQ ID NO:1078) derived from the coding sequence of SEQ ID NO:1077 shown in Figure 1077.

Figure 1079 shows a nucleotide sequence (SEQ ID NO:1079) of a native sequence PRO868 cDNA, wherein SEQ ID NO:1079 is a clone designated herein as "DNA324728".

30       Figure 1080 shows the amino acid sequence (SEQ ID NO:1080) derived from the coding sequence of SEQ ID NO:1079 shown in Figure 1079.

Figure 1081A-B shows a nucleotide sequence (SEQ ID NO:1081) of a native sequence PRO23865 cDNA, wherein SEQ ID NO:1081 is a clone designated herein as "DNA194507".

Figure 1082 shows the amino acid sequence (SEQ ID NO:1082) derived from the coding sequence of SEQ ID NO:1081 shown in Figure 1081A-B.

35       Figure 1083 shows a nucleotide sequence (SEQ ID NO:1083) of a native sequence PRO1573 cDNA, wherein SEQ ID NO:1083 is a clone designated herein as "DNA327817".

Figure 1084 shows the amino acid sequence (SEQ ID NO:1084) derived from the coding sequence of SEQ ID NO:1083 shown in Figure 1083.

40       Figure 1085 shows a nucleotide sequence (SEQ ID NO:1085) of a native sequence PRO83775 cDNA, wherein SEQ ID NO:1085 is a clone designated herein as "DNA327818".

Figure 1086 shows the amino acid sequence (SEQ ID NO:1086) derived from the coding sequence of SEQ ID NO:1085 shown in Figure 1085.

Figure 1087 shows a nucleotide sequence (SEQ ID NO:1087) of a native sequence cDNA, wherein SEQ ID NO:1087 is a clone designated herein as "DNA327819".

5        Figure 1088 shows a nucleotide sequence (SEQ ID NO:1088) of a native sequence PRO83776 cDNA, wherein SEQ ID NO:1088 is a clone designated herein as "DNA327820".

Figure 1089 shows the amino acid sequence (SEQ ID NO:1089) derived from the coding sequence of SEQ ID NO:1088 shown in Figure 1088.

10        Figure 1090A-B shows a nucleotide sequence (SEQ ID NO:1090) of a native sequence PRO83777 cDNA, wherein SEQ ID NO:1090 is a clone designated herein as "DNA327821".

Figure 1091 shows the amino acid sequence (SEQ ID NO:1091) derived from the coding sequence of SEQ ID NO:1090 shown in Figure 1090A-B.

Figure 1092 shows a nucleotide sequence (SEQ ID NO:1092) of a native sequence PRO4676 cDNA, wherein SEQ ID NO:1092 is a clone designated herein as "DNA288259".

15        Figure 1093 shows the amino acid sequence (SEQ ID NO:1093) derived from the coding sequence of SEQ ID NO:1092 shown in Figure 1092.

Figure 1094 shows a nucleotide sequence (SEQ ID NO:1094) of a native sequence cDNA, wherein SEQ ID NO:1094 is a clone designated herein as "DNA271990".

20        Figure 1095A-B shows a nucleotide sequence (SEQ ID NO:1095) of a native sequence cDNA, wherein SEQ ID NO:1095 is a clone designated herein as "DNA273734".

Figure 1096 shows a nucleotide sequence (SEQ ID NO:1096) of a native sequence cDNA, wherein ~~SEQ ID NO:1096 is a clone designated herein as "DNA327822".~~

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Figure 1097 shows a nucleotide sequence (SEQ ID NO:1097) of a native sequence PRO83778 cDNA, wherein SEQ ID NO:1097 is a clone designated herein as "DNA327823".

25        Figure 1098 shows the amino acid sequence (SEQ ID NO:1098) derived from the coding sequence of SEQ ID NO:1097 shown in Figure 1097.

Figure 1099A-B shows a nucleotide sequence (SEQ ID NO:1099) of a native sequence PRO34518 cDNA, wherein SEQ ID NO:1099 is a clone designated herein as "DNA327824".

30        Figure 1100 shows the amino acid sequence (SEQ ID NO:1100) derived from the coding sequence of SEQ ID NO:1099 shown in Figure 1099A-B.

Figure 1101 shows a nucleotide sequence (SEQ ID NO:1101) of a native sequence cDNA, wherein SEQ ID NO:1101 is a clone designated herein as "DNA271933".

Figure 1102A-B shows a nucleotide sequence (SEQ ID NO:1102) of a native sequence PRO83779 cDNA, wherein SEQ ID NO:1102 is a clone designated herein as "DNA327825".

35        Figure 1103 shows the amino acid sequence (SEQ ID NO:1103) derived from the coding sequence of SEQ ID NO:1102 shown in Figure 1102A-B.

Figure 1104A-B shows a nucleotide sequence (SEQ ID NO:1104) of a native sequence PRO24039 cDNA, wherein SEQ ID NO:1104 is a clone designated herein as "DNA327826".

40        Figure 1105 shows the amino acid sequence (SEQ ID NO:1105) derived from the coding sequence of SEQ ID NO:1104 shown in Figure 1104A-B.

Figure 1106 shows a nucleotide sequence (SEQ ID NO:1106) of a native sequence PRO38060 cDNA, wherein SEQ ID NO:1106 is a clone designated herein as "DNA227597".

Figure 1107 shows the amino acid sequence (SEQ ID NO:1107) derived from the coding sequence of SEQ ID NO:1106 shown in Figure 1106.

5        Figure 1108A-B shows a nucleotide sequence (SEQ ID NO:1108) of a native sequence cDNA, wherein SEQ ID NO:1108 is a clone designated herein as "DNA327827".

Figure 1109 shows a nucleotide sequence (SEQ ID NO:1109) of a native sequence PRO83780 cDNA, wherein SEQ ID NO:1109 is a clone designated herein as "DNA327828".

10       Figure 1110 shows the amino acid sequence (SEQ ID NO:1110) derived from the coding sequence of SEQ ID NO:1109 shown in Figure 1109.

Figure 1111 shows a nucleotide sequence (SEQ ID NO:1111) of a native sequence PRO83781 cDNA, wherein SEQ ID NO:1111 is a clone designated herein as "DNA327829".

Figure 1112 shows the amino acid sequence (SEQ ID NO:1112) derived from the coding sequence of SEQ ID NO:1111 shown in Figure 1111.

15       Figure 1113 shows a nucleotide sequence (SEQ ID NO:1113) of a native sequence PRO83782 cDNA, wherein SEQ ID NO:1113 is a clone designated herein as "DNA327830".

Figure 1114 shows the amino acid sequence (SEQ ID NO:1114) derived from the coding sequence of SEQ ID NO:1113 shown in Figure 1113.

20       Figure 1115 shows a nucleotide sequence (SEQ ID NO:1115) of a native sequence PRO83783 cDNA, wherein SEQ ID NO:1115 is a clone designated herein as "DNA327831".

Figure 1116 shows the amino acid sequence (SEQ ID NO:1116) derived from the coding sequence of SEQ ID NO:1115 shown in Figure 1115.

Figure 1117 shows a nucleotide sequence (SEQ ID NO:1117) of a native sequence PRO83784 cDNA, wherein SEQ ID NO:1117 is a clone designated herein as "DNA327832".

25       Figure 1118 shows the amino acid sequence (SEQ ID NO:1118) derived from the coding sequence of SEQ ID NO:1117 shown in Figure 1117.

Figure 1119 shows a nucleotide sequence (SEQ ID NO:1119) of a native sequence PRO23628 cDNA, wherein SEQ ID NO:1119 is a clone designated herein as "DNA327833".

30       Figure 1120 shows the amino acid sequence (SEQ ID NO:1120) derived from the coding sequence of SEQ ID NO:1119 shown in Figure 1119.

Figure 1121A-B shows a nucleotide sequence (SEQ ID NO:1121) of a native sequence PRO83785 cDNA, wherein SEQ ID NO:1121 is a clone designated herein as "DNA327834".

Figure 1122 shows the amino acid sequence (SEQ ID NO:1122) derived from the coding sequence of SEQ ID NO:1121 shown in Figure 1121A-B.

35       Figure 1123A-B shows a nucleotide sequence (SEQ ID NO:1123) of a native sequence PRO83786 cDNA, wherein SEQ ID NO:1123 is a clone designated herein as "DNA327835".

Figure 1124 shows the amino acid sequence (SEQ ID NO:1124) derived from the coding sequence of SEQ ID NO:1123 shown in Figure 1123A-B.

40       Figure 1125 shows a nucleotide sequence (SEQ ID NO:1125) of a native sequence PRO52581 cDNA, wherein SEQ ID NO:1125 is a clone designated herein as "DNA258641".

Figure 1126 shows the amino acid sequence (SEQ ID NO:1126) derived from the coding sequence of SEQ ID NO:1125 shown in Figure 1125.

Figure 1127 shows a nucleotide sequence (SEQ ID NO:1127) of a native sequence PRO83787 cDNA, wherein SEQ ID NO:1127 is a clone designated herein as "DNA327836".

5        Figure 1128 shows the amino acid sequence (SEQ ID NO:1128) derived from the coding sequence of SEQ ID NO:1127 shown in Figure 1127.

Figure 1129A-B shows a nucleotide sequence (SEQ ID NO:1129) of a native sequence PRO49486 cDNA, wherein SEQ ID NO:1129 is a clone designated herein as "DNA254376".

10       Figure 1130 shows the amino acid sequence (SEQ ID NO:1130) derived from the coding sequence of SEQ ID NO:1129 shown in Figure 1129A-B.

Figure 1131 shows a nucleotide sequence (SEQ ID NO:1131) of a native sequence PRO83788 cDNA, wherein SEQ ID NO:1131 is a clone designated herein as "DNA327837".

Figure 1132 shows the amino acid sequence (SEQ ID NO:1132) derived from the coding sequence of SEQ ID NO:1131 shown in Figure 1131.

15       Figure 1133 shows a nucleotide sequence (SEQ ID NO:1133) of a native sequence PRO83789 cDNA, wherein SEQ ID NO:1133 is a clone designated herein as "DNA327838".

Figure 1134 shows the amino acid sequence (SEQ ID NO:1134) derived from the coding sequence of SEQ ID NO:1133 shown in Figure 1133.

20       Figure 1135 shows a nucleotide sequence (SEQ ID NO:1135) of a native sequence PRO38220 cDNA, wherein SEQ ID NO:1135 is a clone designated herein as "DNA227757".

Figure 1136 shows the amino acid sequence (SEQ ID NO:1136) derived from the coding sequence of SEQ ID NO:1135 shown in Figure 1135.

Figure 1137 shows a nucleotide sequence (SEQ ID NO:1137) of a native sequence PRO2730 cDNA, wherein SEQ ID NO:1137 is a clone designated herein as "DNA88292".

25       Figure 1138 shows the amino acid sequence (SEQ ID NO:1138) derived from the coding sequence of SEQ ID NO:1137 shown in Figure 1137.

Figure 1139 shows a nucleotide sequence (SEQ ID NO:1139) of a native sequence PRO21884 cDNA, wherein SEQ ID NO:1139 is a clone designated herein as "DNA188349".

30       Figure 1140 shows the amino acid sequence (SEQ ID NO:1140) derived from the coding sequence of SEQ ID NO:1139 shown in Figure 1139.

Figure 1141 shows a nucleotide sequence (SEQ ID NO:1141) of a native sequence PRO83790 cDNA, wherein SEQ ID NO:1141 is a clone designated herein as "DNA327839".

Figure 1142 shows the amino acid sequence (SEQ ID NO:1142) derived from the coding sequence of SEQ ID NO:1141 shown in Figure 1141.

35       Figure 1143 shows a nucleotide sequence (SEQ ID NO:1143) of a native sequence PRO37826 cDNA, wherein SEQ ID NO:1143 is a clone designated herein as "DNA327840".

Figure 1144 shows the amino acid sequence (SEQ ID NO:1144) derived from the coding sequence of SEQ ID NO:1143 shown in Figure 1143.

40       Figure 1145 shows a nucleotide sequence (SEQ ID NO:1145) of a native sequence PRO58102 cDNA, wherein SEQ ID NO:1145 is a clone designated herein as "DNA269692".

Figure 1146 shows the amino acid sequence (SEQ ID NO:1146) derived from the coding sequence of SEQ ID NO:1145 shown in Figure 1145.

Figure 1147 shows a nucleotide sequence (SEQ ID NO:1147) of a native sequence PRO12377 cDNA, wherein SEQ ID NO:1147 is a clone designated herein as "DNA327841".

5 Figure 1148 shows the amino acid sequence (SEQ ID NO:1148) derived from the coding sequence of SEQ ID NO:1147 shown in Figure 1147.

Figure 1149 shows a nucleotide sequence (SEQ ID NO:1149) of a native sequence PRO36639 cDNA, wherein SEQ ID NO:1149 is a clone designated herein as "DNA226176".

10 Figure 1150 shows the amino acid sequence (SEQ ID NO:1150) derived from the coding sequence of SEQ ID NO:1149 shown in Figure 1149.

Figure 1151 shows a nucleotide sequence (SEQ ID NO:1151) of a native sequence cDNA, wherein SEQ ID NO:1151 is a clone designated herein as "DNA195995".

Figure 1152 shows a nucleotide sequence (SEQ ID NO:1152) of a native sequence PRO83791 cDNA, wherein SEQ ID NO:1152 is a clone designated herein as "DNA327842".

15 Figure 1153 shows the amino acid sequence (SEQ ID NO:1153) derived from the coding sequence of SEQ ID NO:1152 shown in Figure 1152.

Figure 1154 shows a nucleotide sequence (SEQ ID NO:1154) of a native sequence PRO81472 cDNA, wherein SEQ ID NO:1154 is a clone designated herein as "DNA327843".

20 Figure 1155 shows the amino acid sequence (SEQ ID NO:1155) derived from the coding sequence of SEQ ID NO:1154 shown in Figure 1154.

Figure 1156 shows a nucleotide sequence (SEQ ID NO:1156) of a native sequence PRO51365 cDNA, wherein SEQ ID NO:1156 is a clone designated herein as "DNA327844".

Figure 1157 shows the amino acid sequence (SEQ ID NO:1157) derived from the coding sequence of SEQ ID NO:1156 shown in Figure 1156.

25 Figure 1158 shows a nucleotide sequence (SEQ ID NO:1158) of a native sequence PRO69463 cDNA, wherein SEQ ID NO:1158 is a clone designated herein as "DNA287173".

Figure 1159 shows the amino acid sequence (SEQ ID NO:1159) derived from the coding sequence of SEQ ID NO:1158 shown in Figure 1158.

30 Figure 1160 shows a nucleotide sequence (SEQ ID NO:1160) of a native sequence PRO61271 cDNA, wherein SEQ ID NO:1160 is a clone designated herein as "DNA327845".

Figure 1161 shows the amino acid sequence (SEQ ID NO:1161) derived from the coding sequence of SEQ ID NO:1160 shown in Figure 1160.

Figure 1162 shows a nucleotide sequence (SEQ ID NO:1162) of a native sequence cDNA, wherein SEQ ID NO:1162 is a clone designated herein as "DNA196182".

35 Figure 1163 shows a nucleotide sequence (SEQ ID NO:1163) of a native sequence PRO83792 cDNA, wherein SEQ ID NO:1163 is a clone designated herein as "DNA327846".

Figure 1164 shows the amino acid sequence (SEQ ID NO:1164) derived from the coding sequence of SEQ ID NO:1163 shown in Figure 1163.

40 Figure 1165A-B shows a nucleotide sequence (SEQ ID NO:1165) of a native sequence PRO2834 cDNA, wherein SEQ ID NO:1165 is a clone designated herein as "DNA327847".



Figure 1166 shows the amino acid sequence (SEQ ID NO:1166) derived from the coding sequence of SEQ ID NO:1165 shown in Figure 1165A-B.

Figure 1167 shows a nucleotide sequence (SEQ ID NO:1167) of a native sequence PRO2834 cDNA, wherein SEQ ID NO:1167 is a clone designated herein as "DNA88541".

5        Figure 1168 shows the amino acid sequence (SEQ ID NO:1168) derived from the coding sequence of SEQ ID NO:1167 shown in Figure 1167.

Figure 1169 shows a nucleotide sequence (SEQ ID NO:1169) of a native sequence PRO83793 cDNA, wherein SEQ ID NO:1169 is a clone designated herein as "DNA327848".

10       Figure 1170 shows the amino acid sequence (SEQ ID NO:1170) derived from the coding sequence of SEQ ID NO:1169 shown in Figure 1169.

Figure 1171 shows a nucleotide sequence (SEQ ID NO:1171) of a native sequence PRO83794 cDNA, wherein SEQ ID NO:1171 is a clone designated herein as "DNA327849".

Figure 1172 shows the amino acid sequence (SEQ ID NO:1172) derived from the coding sequence of SEQ ID NO:1171 shown in Figure 1171.

15       Figure 1173A-B shows a nucleotide sequence (SEQ ID NO:1173) of a native sequence PRO2237 cDNA, wherein SEQ ID NO:1173 is a clone designated herein as "DNA88226".

Figure 1174 shows the amino acid sequence (SEQ ID NO:1174) derived from the coding sequence of SEQ ID NO:1173 shown in Figure 1173A-B.

20       Figure 1175 shows a nucleotide sequence (SEQ ID NO:1175) of a native sequence PRO60803 cDNA, wherein SEQ ID NO:1175 is a clone designated herein as "DNA327850".

Figure 1176 shows the amino acid sequence (SEQ ID NO:1176) derived from the coding sequence of SEQ ID NO:1175 shown in Figure 1175.

Figure 1177 shows a nucleotide sequence (SEQ ID NO:1177) of a native sequence PRO80741 cDNA, wherein SEQ ID NO:1177 is a clone designated herein as "DNA324022".

25       Figure 1178 shows the amino acid sequence (SEQ ID NO:1178) derived from the coding sequence of SEQ ID NO:1177 shown in Figure 1177.

Figure 1179 shows a nucleotide sequence (SEQ ID NO:1179) of a native sequence PRO83795 cDNA, wherein SEQ ID NO:1179 is a clone designated herein as "DNA327851".

30       Figure 1180 shows the amino acid sequence (SEQ ID NO:1180) derived from the coding sequence of SEQ ID NO:1179 shown in Figure 1179.

Figure 1181 shows a nucleotide sequence (SEQ ID NO:1181) of a native sequence PRO60759 cDNA, wherein SEQ ID NO:1181 is a clone designated herein as "DNA272626".

Figure 1182 shows the amino acid sequence (SEQ ID NO:1182) derived from the coding sequence of SEQ ID NO:1181 shown in Figure 1181.

35       Figure 1183 shows a nucleotide sequence (SEQ ID NO:1183) of a native sequence PRO37222 cDNA, wherein SEQ ID NO:1183 is a clone designated herein as "DNA226759".

Figure 1184 shows the amino acid sequence (SEQ ID NO:1184) derived from the coding sequence of SEQ ID NO:1183 shown in Figure 1183.

40       Figure 1185A-B shows a nucleotide sequence (SEQ ID NO:1185) of a native sequence PRO81523 cDNA, wherein SEQ ID NO:1185 is a clone designated herein as "DNA324921".

Figure 1186 shows the amino acid sequence (SEQ ID NO:1186) derived from the coding sequence of SEQ ID NO:1185 shown in Figure 1185A-B.

Figure 1187 shows a nucleotide sequence (SEQ ID NO:1187) of a native sequence PRO83796 cDNA, wherein SEQ ID NO:1187 is a clone designated herein as "DNA327852".

5        Figure 1188 shows the amino acid sequence (SEQ ID NO:1188) derived from the coding sequence of SEQ ID NO:1187 shown in Figure 1187.

Figure 1189 shows a nucleotide sequence (SEQ ID NO:1189) of a native sequence PRO82223 cDNA, wherein SEQ ID NO:1189 is a clone designated herein as "DNA327853".

10       Figure 1190 shows the amino acid sequence (SEQ ID NO:1190) derived from the coding sequence of SEQ ID NO:1189 shown in Figure 1189.

Figure 1191A-B shows a nucleotide sequence (SEQ ID NO:1191) of a native sequence PRO83797 cDNA, wherein SEQ ID NO:1191 is a clone designated herein as "DNA327854".

Figure 1192 shows the amino acid sequence (SEQ ID NO:1192) derived from the coding sequence of SEQ ID NO:1191 shown in Figure 1191A-B.

15       Figure 1193 shows a nucleotide sequence (SEQ ID NO:1193) of a native sequence PRO83367 cDNA, wherein SEQ ID NO:1193 is a clone designated herein as "DNA327855".

Figure 1194 shows the amino acid sequence (SEQ ID NO:1194) derived from the coding sequence of SEQ ID NO:1193 shown in Figure 1193.

20       Figure 1195 shows a nucleotide sequence (SEQ ID NO:1195) of a native sequence PRO61079 cDNA, wherein SEQ ID NO:1195 is a clone designated herein as "DNA273008".

Figure 1196 shows the amino acid sequence (SEQ ID NO:1196) derived from the coding sequence of SEQ ID NO:1195 shown in Figure 1195.

Figure 1197A-B shows a nucleotide sequence (SEQ ID NO:1197) of a native sequence PRO83798 cDNA, wherein SEQ ID NO:1197 is a clone designated herein as "DNA327856".

25       Figure 1198 shows the amino acid sequence (SEQ ID NO:1198) derived from the coding sequence of SEQ ID NO:1197 shown in Figure 1197A-B.

Figure 1199 shows a nucleotide sequence (SEQ ID NO:1199) of a native sequence PRO37776 cDNA, wherein SEQ ID NO:1199 is a clone designated herein as "DNA227313".

30       Figure 1200 shows the amino acid sequence (SEQ ID NO:1200) derived from the coding sequence of SEQ ID NO:1199 shown in Figure 1199.

Figure 1201 shows a nucleotide sequence (SEQ ID NO:1201) of a native sequence PRO37961 cDNA, wherein SEQ ID NO:1201 is a clone designated herein as "DNA227498".

Figure 1202 shows the amino acid sequence (SEQ ID NO:1202) derived from the coding sequence of SEQ ID NO:1201 shown in Figure 1201.

35       Figure 1203 shows a nucleotide sequence (SEQ ID NO:1203) of a native sequence PRO83799 cDNA, wherein SEQ ID NO:1203 is a clone designated herein as "DNA327857".

Figure 1204 shows the amino acid sequence (SEQ ID NO:1204) derived from the coding sequence of SEQ ID NO:1203 shown in Figure 1203.

40       Figure 1205 shows a nucleotide sequence (SEQ ID NO:1205) of a native sequence PRO49837 cDNA, wherein SEQ ID NO:1205 is a clone designated herein as "DNA254739".

Figure 1206 shows the amino acid sequence (SEQ ID NO:1206) derived from the coding sequence of SEQ ID NO:1205 shown in Figure 1205.

Figure 1207 shows a nucleotide sequence (SEQ ID NO:1207) of a native sequence PRO83800 cDNA, wherein SEQ ID NO:1207 is a clone designated herein as "DNA327858".

5        Figure 1208 shows the amino acid sequence (SEQ ID NO:1208) derived from the coding sequence of SEQ ID NO:1207 shown in Figure 1207.

Figure 1209 shows a nucleotide sequence (SEQ ID NO:1209) of a native sequence PRO69677 cDNA, wherein SEQ ID NO:1209 is a clone designated herein as "DNA287420".

10       Figure 1210 shows the amino acid sequence (SEQ ID NO:1210) derived from the coding sequence of SEQ ID NO:1209 shown in Figure 1209.

Figure 1211 shows a nucleotide sequence (SEQ ID NO:1211) of a native sequence PRO37748 cDNA, wherein SEQ ID NO:1211 is a clone designated herein as "DNA327859".

Figure 1212 shows the amino acid sequence (SEQ ID NO:1212) derived from the coding sequence of SEQ ID NO:1211 shown in Figure 1211.

15       Figure 1213 shows a nucleotide sequence (SEQ ID NO:1213) of a native sequence PRO83801 cDNA, wherein SEQ ID NO:1213 is a clone designated herein as "DNA327860".

Figure 1214 shows the amino acid sequence (SEQ ID NO:1214) derived from the coding sequence of SEQ ID NO:1213 shown in Figure 1213.

20       Figure 1215 shows a nucleotide sequence (SEQ ID NO:1215) of a native sequence PRO83802 cDNA, wherein SEQ ID NO:1215 is a clone designated herein as "DNA327861".

Figure 1216 shows the amino acid sequence (SEQ ID NO:1216) derived from the coding sequence of SEQ ID NO:1215 shown in Figure 1215.

Figure 1217 shows a nucleotide sequence (SEQ ID NO:1217) of a native sequence PRO83803 cDNA, wherein SEQ ID NO:1217 is a clone designated herein as "DNA327862".

25       Figure 1218 shows the amino acid sequence (SEQ ID NO:1218) derived from the coding sequence of SEQ ID NO:1217 shown in Figure 1217.

Figure 1219 shows a nucleotide sequence (SEQ ID NO:1219) of a native sequence PRO83804 cDNA, wherein SEQ ID NO:1219 is a clone designated herein as "DNA327863".

30       Figure 1220 shows the amino acid sequence (SEQ ID NO:1220) derived from the coding sequence of SEQ ID NO:1219 shown in Figure 1219.

Figure 1221 shows a nucleotide sequence (SEQ ID NO:1221) of a native sequence PRO50409 cDNA, wherein SEQ ID NO:1221 is a clone designated herein as "DNA255340".

Figure 1222 shows the amino acid sequence (SEQ ID NO:1222) derived from the coding sequence of SEQ ID NO:1221 shown in Figure 1221.

35       Figure 1223A-B shows a nucleotide sequence (SEQ ID NO:1223) of a native sequence PRO69478 cDNA, wherein SEQ ID NO:1223 is a clone designated herein as "DNA287192".

Figure 1224 shows the amino acid sequence (SEQ ID NO:1224) derived from the coding sequence of SEQ ID NO:1223 shown in Figure 1223A-B.

40       Figure 1225 shows a nucleotide sequence (SEQ ID NO:1225) of a native sequence PRO83805 cDNA, wherein SEQ ID NO:1225 is a clone designated herein as "DNA327864".

Figure 1226 shows the amino acid sequence (SEQ ID NO:1226) derived from the coding sequence of SEQ ID NO:1225 shown in Figure 1225.

Figure 1227 shows a nucleotide sequence (SEQ ID NO:1227) of a native sequence PRO83806 cDNA, wherein SEQ ID NO:1227 is a clone designated herein as "DNA327865".

5        Figure 1228 shows the amino acid sequence (SEQ ID NO:1228) derived from the coding sequence of SEQ ID NO:1227 shown in Figure 1227.

Figure 1229 shows a nucleotide sequence (SEQ ID NO:1229) of a native sequence PRO83807 cDNA, wherein SEQ ID NO:1229 is a clone designated herein as "DNA327866".

10       Figure 1230 shows the amino acid sequence (SEQ ID NO:1230) derived from the coding sequence of SEQ ID NO:1229 shown in Figure 1229.

Figure 1231 shows a nucleotide sequence (SEQ ID NO:1231) of a native sequence PRO83808 cDNA, wherein SEQ ID NO:1231 is a clone designated herein as "DNA327867".

Figure 1232 shows the amino acid sequence (SEQ ID NO:1232) derived from the coding sequence of SEQ ID NO:1231 shown in Figure 1231.

15       Figure 1233 shows a nucleotide sequence (SEQ ID NO:1233) of a native sequence PRO83809 cDNA, wherein SEQ ID NO:1233 is a clone designated herein as "DNA327868".

Figure 1234 shows the amino acid sequence (SEQ ID NO:1234) derived from the coding sequence of SEQ ID NO:1233 shown in Figure 1233.

20       Figure 1235 shows a nucleotide sequence (SEQ ID NO:1235) of a native sequence PRO1898 cDNA, wherein SEQ ID NO:1235 is a clone designated herein as "DNA327869".

Figure 1236 shows the amino acid sequence (SEQ ID NO:1236) derived from the coding sequence of SEQ ID NO:1235 shown in Figure 1235.

Figure 1237 shows a nucleotide sequence (SEQ ID NO:1237) of a native sequence PRO83810 cDNA, wherein SEQ ID NO:1237 is a clone designated herein as "DNA327870".

25       Figure 1238 shows the amino acid sequence (SEQ ID NO:1238) derived from the coding sequence of SEQ ID NO:1237 shown in Figure 1237.

Figure 1239 shows a nucleotide sequence (SEQ ID NO:1239) of a native sequence PRO60668 cDNA, wherein SEQ ID NO:1239 is a clone designated herein as "DNA272415".

30       Figure 1240 shows the amino acid sequence (SEQ ID NO:1240) derived from the coding sequence of SEQ ID NO:1239 shown in Figure 1239.

Figure 1241 shows a nucleotide sequence (SEQ ID NO:1241) of a native sequence PRO37056 cDNA, wherein SEQ ID NO:1241 is a clone designated herein as "DNA226593".

Figure 1242 shows the amino acid sequence (SEQ ID NO:1242) derived from the coding sequence of SEQ ID NO:1241 shown in Figure 1241.

35       Figure 1243 shows a nucleotide sequence (SEQ ID NO:1243) of a native sequence PRO83811 cDNA, wherein SEQ ID NO:1243 is a clone designated herein as "DNA327871".

Figure 1244 shows the amino acid sequence (SEQ ID NO:1244) derived from the coding sequence of SEQ ID NO:1243 shown in Figure 1243.

40       Figure 1245 shows a nucleotide sequence (SEQ ID NO:1245) of a native sequence PRO50616 cDNA, wherein SEQ ID NO:1245 is a clone designated herein as "DNA255552".

Figure 1246 shows the amino acid sequence (SEQ ID NO:1246) derived from the coding sequence of SEQ ID NO:1245 shown in Figure 1245.

Figure 1247 shows a nucleotide sequence (SEQ ID NO:1247) of a native sequence PRO83812 cDNA, wherein SEQ ID NO:1247 is a clone designated herein as "DNA327872".

5 Figure 1248 shows the amino acid sequence (SEQ ID NO:1248) derived from the coding sequence of SEQ ID NO:1247 shown in Figure 1247.

Figure 1249 shows a nucleotide sequence (SEQ ID NO:1249) of a native sequence PRO83813 cDNA, wherein SEQ ID NO:1249 is a clone designated herein as "DNA327873".

10 Figure 1250 shows the amino acid sequence (SEQ ID NO:1250) derived from the coding sequence of SEQ ID NO:1249 shown in Figure 1249.

Figure 1251 shows a nucleotide sequence (SEQ ID NO:1251) of a native sequence PRO4805 cDNA, wherein SEQ ID NO:1251 is a clone designated herein as "DNA327874".

Figure 1252 shows the amino acid sequence (SEQ ID NO:1252) derived from the coding sequence of SEQ ID NO:1251 shown in Figure 1251.

15 Figure 1253 shows a nucleotide sequence (SEQ ID NO:1253) of a native sequence PRO69459 cDNA, wherein SEQ ID NO:1253 is a clone designated herein as "DNA287166".

Figure 1254 shows the amino acid sequence (SEQ ID NO:1254) derived from the coding sequence of SEQ ID NO:1253 shown in Figure 1253.

20 Figure 1255 shows a nucleotide sequence (SEQ ID NO:1255) of a native sequence PRO83814 cDNA, wherein SEQ ID NO:1255 is a clone designated herein as "DNA327875".

Figure 1256 shows the amino acid sequence (SEQ ID NO:1256) derived from the coding sequence of SEQ ID NO:1255 shown in Figure 1255.

Figure 1257 shows a nucleotide sequence (SEQ ID NO:1257) of a native sequence PRO66032 cDNA, wherein SEQ ID NO:1257 is a clone designated herein as "DNA279661".

25 Figure 1258 shows the amino acid sequence (SEQ ID NO:1258) derived from the coding sequence of SEQ ID NO:1257 shown in Figure 1257.

Figure 1259 shows a nucleotide sequence (SEQ ID NO:1259) of a native sequence PRO51309 cDNA, wherein SEQ ID NO:1259 is a clone designated herein as "DNA256265".

30 Figure 1260 shows the amino acid sequence (SEQ ID NO:1260) derived from the coding sequence of SEQ ID NO:1259 shown in Figure 1259.

Figure 1261 shows a nucleotide sequence (SEQ ID NO:1261) of a native sequence PRO83469 cDNA, wherein SEQ ID NO:1261 is a clone designated herein as "DNA327191".

Figure 1262 shows the amino acid sequence (SEQ ID NO:1262) derived from the coding sequence of SEQ ID NO:1261 shown in Figure 1261.

35 Figure 1263 shows a nucleotide sequence (SEQ ID NO:1263) of a native sequence PRO83815 cDNA, wherein SEQ ID NO:1263 is a clone designated herein as "DNA327876".

Figure 1264 shows the amino acid sequence (SEQ ID NO:1264) derived from the coding sequence of SEQ ID NO:1263 shown in Figure 1263.

40 Figure 1265 shows a nucleotide sequence (SEQ ID NO:1265) of a native sequence PRO83816 cDNA, wherein SEQ ID NO:1265 is a clone designated herein as "DNA327877".

Figure 1266 shows the amino acid sequence (SEQ ID NO:1266) derived from the coding sequence of SEQ ID NO:1265 shown in Figure 1265.

Figure 1267 shows a nucleotide sequence (SEQ ID NO:1267) of a native sequence PRO34321 cDNA, wherein SEQ ID NO:1267 is a clone designated herein as "DNA218269".

5        Figure 1268 shows the amino acid sequence (SEQ ID NO:1268) derived from the coding sequence of SEQ ID NO:1267 shown in Figure 1267.

Figure 1269 shows a nucleotide sequence (SEQ ID NO:1269) of a native sequence PRO70808 cDNA, wherein SEQ ID NO:1269 is a clone designated herein as "DNA297191".

10       Figure 1270 shows the amino acid sequence (SEQ ID NO:1270) derived from the coding sequence of SEQ ID NO:1269 shown in Figure 1269.

Figure 1271 shows a nucleotide sequence (SEQ ID NO:1271) of a native sequence PRO83817 cDNA, wherein SEQ ID NO:1271 is a clone designated herein as "DNA327878".

Figure 1272 shows the amino acid sequence (SEQ ID NO:1272) derived from the coding sequence of SEQ ID NO:1271 shown in Figure 1271.

15       Figure 1273 shows a nucleotide sequence (SEQ ID NO:1273) of a native sequence PRO83818 cDNA, wherein SEQ ID NO:1273 is a clone designated herein as "DNA327879".

Figure 1274 shows the amino acid sequence (SEQ ID NO:1274) derived from the coding sequence of SEQ ID NO:1273 shown in Figure 1273.

20       Figure 1275 shows a nucleotide sequence (SEQ ID NO:1275) of a native sequence PRO83819 cDNA, wherein SEQ ID NO:1275 is a clone designated herein as "DNA327880".

Figure 1276 shows the amino acid sequence (SEQ ID NO:1276) derived from the coding sequence of SEQ ID NO:1275 shown in Figure 1275.

Figure 1277 shows a nucleotide sequence (SEQ ID NO:1277) of a native sequence PRO83820 cDNA, wherein SEQ ID NO:1277 is a clone designated herein as "DNA327881".

25       Figure 1278 shows the amino acid sequence (SEQ ID NO:1278) derived from the coding sequence of SEQ ID NO:1277 shown in Figure 1277.

Figure 1279 shows a nucleotide sequence (SEQ ID NO:1279) of a native sequence PRO31794 cDNA, wherein SEQ ID NO:1279 is a clone designated herein as "DNA327882".

30       Figure 1280 shows the amino acid sequence (SEQ ID NO:1280) derived from the coding sequence of SEQ ID NO:1279 shown in Figure 1279.

Figure 1281 shows a nucleotide sequence (SEQ ID NO:1281) of a native sequence PRO82421 cDNA, wherein SEQ ID NO:1281 is a clone designated herein as "DNA325976".

Figure 1282 shows the amino acid sequence (SEQ ID NO:1282) derived from the coding sequence of SEQ ID NO:1281 shown in Figure 1281.

35       Figure 1283 shows a nucleotide sequence (SEQ ID NO:1283) of a native sequence PRO49810 cDNA, wherein SEQ ID NO:1283 is a clone designated herein as "DNA254710".

Figure 1284 shows the amino acid sequence (SEQ ID NO:1284) derived from the coding sequence of SEQ ID NO:1283 shown in Figure 1283.

40       Figure 1285 shows a nucleotide sequence (SEQ ID NO:1285) of a native sequence PRO59776 cDNA, wherein SEQ ID NO:1285 is a clone designated herein as "DNA271483".

Figure 1286 shows the amino acid sequence (SEQ ID NO:1286) derived from the coding sequence of SEQ ID NO:1285 shown in Figure 1285.

Figure 1287 shows a nucleotide sequence (SEQ ID NO:1287) of a native sequence PRO83821 cDNA, wherein SEQ ID NO:1287 is a clone designated herein as "DNA327883".

5        Figure 1288 shows the amino acid sequence (SEQ ID NO:1288) derived from the coding sequence of SEQ ID NO:1287 shown in Figure 1287.

Figure 1289 shows a nucleotide sequence (SEQ ID NO:1289) of a native sequence PRO83822 cDNA, wherein SEQ ID NO:1289 is a clone designated herein as "DNA327884".

10       Figure 1290 shows the amino acid sequence (SEQ ID NO:1290) derived from the coding sequence of SEQ ID NO:1289 shown in Figure 1289.

Figure 1291 shows a nucleotide sequence (SEQ ID NO:1291) of a native sequence PRO82377 cDNA, wherein SEQ ID NO:1291 is a clone designated herein as "DNA327885".

Figure 1292 shows the amino acid sequence (SEQ ID NO:1292) derived from the coding sequence of SEQ ID NO:1291 shown in Figure 1291.

15       Figure 1293 shows a nucleotide sequence (SEQ ID NO:1293) of a native sequence PRO41077 cDNA, wherein SEQ ID NO:1293 is a clone designated herein as "DNA327886".

Figure 1294 shows the amino acid sequence (SEQ ID NO:1294) derived from the coding sequence of SEQ ID NO:1293 shown in Figure 1293.

20       Figure 1295 shows a nucleotide sequence (SEQ ID NO:1295) of a native sequence PRO83823 cDNA, wherein SEQ ID NO:1295 is a clone designated herein as "DNA327887".

Figure 1296 shows the amino acid sequence (SEQ ID NO:1296) derived from the coding sequence of SEQ ID NO:1295 shown in Figure 1295.

Figure 1297 shows a nucleotide sequence (SEQ ID NO:1297) of a native sequence PRO83824 cDNA, wherein SEQ ID NO:1297 is a clone designated herein as "DNA327888".

25       Figure 1298 shows the amino acid sequence (SEQ ID NO:1298) derived from the coding sequence of SEQ ID NO:1297 shown in Figure 1297.

Figure 1299 shows a nucleotide sequence (SEQ ID NO:1299) of a native sequence PRO83825 cDNA, wherein SEQ ID NO:1299 is a clone designated herein as "DNA327889".

30       Figure 1300 shows the amino acid sequence (SEQ ID NO:1300) derived from the coding sequence of SEQ ID NO:1299 shown in Figure 1299.

Figure 1301 shows a nucleotide sequence (SEQ ID NO:1301) of a native sequence PRO83826 cDNA, wherein SEQ ID NO:1301 is a clone designated herein as "DNA327890".

Figure 1302 shows the amino acid sequence (SEQ ID NO:1302) derived from the coding sequence of SEQ ID NO:1301 shown in Figure 1301.

35       Figure 1303 shows a nucleotide sequence (SEQ ID NO:1303) of a native sequence PRO50546 cDNA, wherein SEQ ID NO:1303 is a clone designated herein as "DNA255479".

Figure 1304 shows the amino acid sequence (SEQ ID NO:1304) derived from the coding sequence of SEQ ID NO:1303 shown in Figure 1303.

40       Figure 1305 shows a nucleotide sequence (SEQ ID NO:1305) of a native sequence PRO83827 cDNA, wherein SEQ ID NO:1305 is a clone designated herein as "DNA327891".

Figure 1306 shows the amino acid sequence (SEQ ID NO:1306) derived from the coding sequence of SEQ ID NO:1305 shown in Figure 1305.

Figure 1307 shows a nucleotide sequence (SEQ ID NO:1307) of a native sequence PRO37408 cDNA, wherein SEQ ID NO:1307 is a clone designated herein as "DNA226945".

5        Figure 1308 shows the amino acid sequence (SEQ ID NO:1308) derived from the coding sequence of SEQ ID NO:1307 shown in Figure 1307.

Figure 1309 shows a nucleotide sequence (SEQ ID NO:1309) of a native sequence PRO83828 cDNA, wherein SEQ ID NO:1309 is a clone designated herein as "DNA327892".

10       Figure 1310 shows the amino acid sequence (SEQ ID NO:1310) derived from the coding sequence of SEQ ID NO:1309 shown in Figure 1309.

Figure 1311 shows a nucleotide sequence (SEQ ID NO:1311) of a native sequence PRO83829 cDNA, wherein SEQ ID NO:1311 is a clone designated herein as "DNA327893".

Figure 1312 shows the amino acid sequence (SEQ ID NO:1312) derived from the coding sequence of SEQ ID NO:1311 shown in Figure 1311.

15       Figure 1313 shows a nucleotide sequence (SEQ ID NO:1313) of a native sequence PRO50241 cDNA, wherein SEQ ID NO:1313 is a clone designated herein as "DNA255161".

Figure 1314 shows the amino acid sequence (SEQ ID NO:1314) derived from the coding sequence of SEQ ID NO:1313 shown in Figure 1313.

20       Figure 1315 shows a nucleotide sequence (SEQ ID NO:1315) of a native sequence PRO37102 cDNA, wherein SEQ ID NO:1315 is a clone designated herein as "DNA226639".

Figure 1316 shows the amino acid sequence (SEQ ID NO:1316) derived from the coding sequence of SEQ ID NO:1315 shown in Figure 1315.

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Figure 1317 shows a nucleotide sequence (SEQ ID NO:1317) of a native sequence PRO69488 cDNA, wherein SEQ ID NO:1317 is a clone designated herein as "DNA287206".

25       Figure 1318 shows the amino acid sequence (SEQ ID NO:1318) derived from the coding sequence of SEQ ID NO:1317 shown in Figure 1317.

Figure 1319 shows a nucleotide sequence (SEQ ID NO:1319) of a native sequence PRO83830 cDNA, wherein SEQ ID NO:1319 is a clone designated herein as "DNA327894".

30       Figure 1320 shows the amino acid sequence (SEQ ID NO:1320) derived from the coding sequence of SEQ ID NO:1319 shown in Figure 1319.

Figure 1321 shows a nucleotide sequence (SEQ ID NO:1321) of a native sequence PRO83831 cDNA, wherein SEQ ID NO:1321 is a clone designated herein as "DNA327895".

Figure 1322 shows the amino acid sequence (SEQ ID NO:1322) derived from the coding sequence of SEQ ID NO:1321 shown in Figure 1321.

35       Figure 1323 shows a nucleotide sequence (SEQ ID NO:1323) of a native sequence PRO83832 cDNA, wherein SEQ ID NO:1323 is a clone designated herein as "DNA327896".

Figure 1324 shows the amino acid sequence (SEQ ID NO:1324) derived from the coding sequence of SEQ ID NO:1323 shown in Figure 1323.

40       Figure 1325 shows a nucleotide sequence (SEQ ID NO:1325) of a native sequence PRO33675 cDNA, wherein SEQ ID NO:1325 is a clone designated herein as "DNA210130".



Figure 1326 shows the amino acid sequence (SEQ ID NO:1326) derived from the coding sequence of SEQ ID NO:1325 shown in Figure 1325.

Figure 1327 shows a nucleotide sequence (SEQ ID NO:1327) of a native sequence PRO83833 cDNA, wherein SEQ ID NO:1327 is a clone designated herein as "DNA327897".

5        Figure 1328 shows the amino acid sequence (SEQ ID NO:1328) derived from the coding sequence of SEQ ID NO:1327 shown in Figure 1327.

Figure 1329 shows a nucleotide sequence (SEQ ID NO:1329) of a native sequence PRO38467 cDNA, wherein SEQ ID NO:1329 is a clone designated herein as "DNA228004".

10       Figure 1330 shows the amino acid sequence (SEQ ID NO:1330) derived from the coding sequence of SEQ ID NO:1329 shown in Figure 1329.

Figure 1331 shows a nucleotide sequence (SEQ ID NO:1331) of a native sequence PRO38250 cDNA, wherein SEQ ID NO:1331 is a clone designated herein as "DNA227787".

Figure 1332 shows the amino acid sequence (SEQ ID NO:1332) derived from the coding sequence of SEQ ID NO:1331 shown in Figure 1331.

15       Figure 1333 shows a nucleotide sequence (SEQ ID NO:1333) of a native sequence PRO38854 cDNA, wherein SEQ ID NO:1333 is a clone designated herein as "DNA327898".

Figure 1334 shows the amino acid sequence (SEQ ID NO:1334) derived from the coding sequence of SEQ ID NO:1333 shown in Figure 1333.

20       Figure 1335 shows a nucleotide sequence (SEQ ID NO:1335) of a native sequence PRO82424 cDNA, wherein SEQ ID NO:1335 is a clone designated herein as "DNA325979".

Figure 1336 shows the amino acid sequence (SEQ ID NO:1336) derived from the coding sequence of SEQ ID NO:1335 shown in Figure 1335.

Figure 1337 shows a nucleotide sequence (SEQ ID NO:1337) of a native sequence PRO83834 cDNA, wherein SEQ ID NO:1337 is a clone designated herein as "DNA327899".

25       Figure 1338 shows the amino acid sequence (SEQ ID NO:1338) derived from the coding sequence of SEQ ID NO:1337 shown in Figure 1337.

Figure 1339 shows a nucleotide sequence (SEQ ID NO:1339) of a native sequence PRO51573 cDNA, wherein SEQ ID NO:1339 is a clone designated herein as "DNA256541".

30       Figure 1340 shows the amino acid sequence (SEQ ID NO:140) derived from the coding sequence of SEQ ID NO:1339 shown in Figure 1339.

Figure 1341 shows a nucleotide sequence (SEQ ID NO:1341) of a native sequence PRO34753 cDNA, wherein SEQ ID NO:1341 is a clone designated herein as "DNA221079".

Figure 1342 shows the amino acid sequence (SEQ ID NO:1342) derived from the coding sequence of SEQ ID NO:1341 shown in Figure 1341.

35       Figure 1343 shows a nucleotide sequence (SEQ ID NO:1343) of a native sequence PRO83835 cDNA, wherein SEQ ID NO:1343 is a clone designated herein as "DNA327900".

Figure 1344 shows the amino acid sequence (SEQ ID NO:1344) derived from the coding sequence of SEQ ID NO:1343 shown in Figure 1343.

40       Figure 1345 shows a nucleotide sequence (SEQ ID NO:1345) of a native sequence PRO83836 cDNA, wherein SEQ ID NO:1345 is a clone designated herein as "DNA327901".

Figure 1346 shows the amino acid sequence (SEQ ID NO:1346) derived from the coding sequence of SEQ ID NO:1345 shown in Figure 1345.

Figure 1347 shows a nucleotide sequence (SEQ ID NO:1347) of a native sequence PRO83837 cDNA, wherein SEQ ID NO:1347 is a clone designated herein as "DNA327902".

5        Figure 1348 shows the amino acid sequence (SEQ ID NO:1348) derived from the coding sequence of SEQ ID NO:1347 shown in Figure 1347.

Figure 1349 shows a nucleotide sequence (SEQ ID NO:1349) of a native sequence PRO83838 cDNA, wherein SEQ ID NO:1349 is a clone designated herein as "DNA327903".

10       Figure 1350 shows the amino acid sequence (SEQ ID NO:1350) derived from the coding sequence of SEQ ID NO:1349 shown in Figure 1349.

Figure 1351 shows a nucleotide sequence (SEQ ID NO:1351) of a native sequence PRO83839 cDNA, wherein SEQ ID NO:1351 is a clone designated herein as "DNA327904".

Figure 1352 shows the amino acid sequence (SEQ ID NO:1352) derived from the coding sequence of SEQ ID NO:1351 shown in Figure 1351.

15       Figure 1353 shows a nucleotide sequence (SEQ ID NO:1353) of a native sequence PRO51567 cDNA, wherein SEQ ID NO:1353 is a clone designated herein as "DNA256535".

Figure 1354 shows the amino acid sequence (SEQ ID NO:1354) derived from the coding sequence of SEQ ID NO:1353 shown in Figure 1353.

20       Figure 1355 shows a nucleotide sequence (SEQ ID NO:1355) of a native sequence PRO49407 cDNA, wherein SEQ ID NO:1355 is a clone designated herein as "DNA254296".

Figure 1356 shows the amino acid sequence (SEQ ID NO:1356) derived from the coding sequence of SEQ ID NO:1355 shown in Figure 1355.

Figure 1357 shows a nucleotide sequence (SEQ ID NO:1357) of a native sequence PRO83840 cDNA, wherein SEQ ID NO:1357 is a clone designated herein as "DNA327905".

25       Figure 1358 shows the amino acid sequence (SEQ ID NO:1358) derived from the coding sequence of SEQ ID NO:1357 shown in Figure 1357.

Figure 1359 shows a nucleotide sequence (SEQ ID NO:1359) of a native sequence PRO51079 cDNA, wherein SEQ ID NO:1359 is a clone designated herein as "DNA256031".

30       Figure 1360 shows the amino acid sequence (SEQ ID NO:1360) derived from the coding sequence of SEQ ID NO:1359 shown in Figure 1359.

Figure 1361 shows a nucleotide sequence (SEQ ID NO:1361) of a native sequence PRO83841 cDNA, wherein SEQ ID NO:1361 is a clone designated herein as "DNA327906".

Figure 1362 shows the amino acid sequence (SEQ ID NO:1362) derived from the coding sequence of SEQ ID NO:1361 shown in Figure 1361.

35       Figure 1363 shows a nucleotide sequence (SEQ ID NO:1363) of a native sequence PRO83842 cDNA, wherein SEQ ID NO:1363 is a clone designated herein as "DNA327907".

Figure 1364 shows the amino acid sequence (SEQ ID NO:1364) derived from the coding sequence of SEQ ID NO:1363 shown in Figure 1363.

40       Figure 1365 shows a nucleotide sequence (SEQ ID NO:1365) of a native sequence PRO37831 cDNA, wherein SEQ ID NO:1365 is a clone designated herein as "DNA227368".

Figure 1366 shows the amino acid sequence (SEQ ID NO:1366) derived from the coding sequence of SEQ ID NO:1365 shown in Figure 1365.

Figure 1367 shows a nucleotide sequence (SEQ ID NO:1367) of a native sequence PRO83843 cDNA, wherein SEQ ID NO:1367 is a clone designated herein as "DNA327908".

5        Figure 1368 shows the amino acid sequence (SEQ ID NO:1368) derived from the coding sequence of SEQ ID NO:1367 shown in Figure 1367.

Figure 1369 shows a nucleotide sequence (SEQ ID NO:1369) of a native sequence PRO83844 cDNA, wherein SEQ ID NO:1369 is a clone designated herein as "DNA327909".

10       Figure 1370 shows the amino acid sequence (SEQ ID NO:1370) derived from the coding sequence of SEQ ID NO:1369 shown in Figure 1369.

Figure 1371 shows a nucleotide sequence (SEQ ID NO:1371) of a native sequence PRO83845 cDNA, wherein SEQ ID NO:1371 is a clone designated herein as "DNA327910".

Figure 1372 shows the amino acid sequence (SEQ ID NO:1372) derived from the coding sequence of SEQ ID NO:1371 shown in Figure 1371.

15       Figure 1373 shows a nucleotide sequence (SEQ ID NO:1373) of a native sequence PRO83846 cDNA, wherein SEQ ID NO:1373 is a clone designated herein as "DNA327911".

Figure 1374 shows the amino acid sequence (SEQ ID NO:1374) derived from the coding sequence of SEQ ID NO:1373 shown in Figure 1373.

20       Figure 1375 shows a nucleotide sequence (SEQ ID NO:1375) of a native sequence PRO83847 cDNA, wherein SEQ ID NO:1375 is a clone designated herein as "DNA327912".

Figure 1376 shows the amino acid sequence (SEQ ID NO:1376) derived from the coding sequence of SEQ ID NO:1375 shown in Figure 1375.

Figure 1377 shows a nucleotide sequence (SEQ ID NO:1377) of a native sequence PRO83848 cDNA, wherein SEQ ID NO:1377 is a clone designated herein as "DNA327913".

25       Figure 1378 shows the amino acid sequence (SEQ ID NO:1378) derived from the coding sequence of SEQ ID NO:1377 shown in Figure 1377.

Figure 1379 shows a nucleotide sequence (SEQ ID NO:1379) of a native sequence PRO83849 cDNA, wherein SEQ ID NO:1379 is a clone designated herein as "DNA327914".

30       Figure 1380 shows the amino acid sequence (SEQ ID NO:1379) derived from the coding sequence of SEQ ID NO:1380 shown in Figure 1380.

Figure 1381 shows a nucleotide sequence (SEQ ID NO:1381) of a native sequence PRO50532 cDNA, wherein SEQ ID NO:1381 is a clone designated herein as "DNA255465".

Figure 1382 shows the amino acid sequence (SEQ ID NO:1382) derived from the coding sequence of SEQ ID NO:1381 shown in Figure 1381.

35       Figure 1383 shows a nucleotide sequence (SEQ ID NO:1383) of a native sequence PRO83850 cDNA, wherein SEQ ID NO:1383 is a clone designated herein as "DNA327915".

Figure 1384 shows the amino acid sequence (SEQ ID NO:1384) derived from the coding sequence of SEQ ID NO:1383 shown in Figure 1383.

40       Figure 1385 shows a nucleotide sequence (SEQ ID NO:1385) of a native sequence PRO50821 cDNA, wherein SEQ ID NO:1385 is a clone designated herein as "DNA255766".

Figure 1386 shows the amino acid sequence (SEQ ID NO:1386) derived from the coding sequence of SEQ ID NO:1385 shown in Figure .

Figure 1387 shows a nucleotide sequence (SEQ ID NO:1387) of a native sequence PRO70011 cDNA, wherein SEQ ID NO:1387 is a clone designated herein as "DNA288247".

5        Figure 1388 shows the amino acid sequence (SEQ ID NO:1388) derived from the coding sequence of SEQ ID NO:1387 shown in Figure 1387.

Figure 1389 shows a nucleotide sequence (SEQ ID NO:1389) of a native sequence PRO83851 cDNA, wherein SEQ ID NO:1389 is a clone designated herein as "DNA327916".

10       Figure 1390 shows the amino acid sequence (SEQ ID NO:1390) derived from the coding sequence of SEQ ID NO:1389 shown in Figure 1389.

Figure 1391 shows a nucleotide sequence (SEQ ID NO:1391) of a native sequence PRO83852 cDNA, wherein SEQ ID NO:1391 is a clone designated herein as "DNA327917".

Figure 1392 shows the amino acid sequence (SEQ ID NO:1392) derived from the coding sequence of SEQ ID NO:1391 shown in Figure 1391.

15       Figure 1393 shows a nucleotide sequence (SEQ ID NO:1393) of a native sequence PRO83853 cDNA, wherein SEQ ID NO:1393 is a clone designated herein as "DNA327918".

Figure 1394 shows the amino acid sequence (SEQ ID NO:1394) derived from the coding sequence of SEQ ID NO:1393 shown in Figure 1393.

20       Figure 1395 shows a nucleotide sequence (SEQ ID NO:1395) of a native sequence PRO83854 cDNA, wherein SEQ ID NO:1395 is a clone designated herein as "DNA327919".

Figure 1396 shows the amino acid sequence (SEQ ID NO:1396) derived from the coding sequence of SEQ ID NO:1395 shown in Figure 1395.

Figure 1397 shows a nucleotide sequence (SEQ ID NO:1397) of a native sequence PRO37730 cDNA, wherein SEQ ID NO:1397 is a clone designated herein as "DNA227267".

25       Figure 1398 shows the amino acid sequence (SEQ ID NO:1398) derived from the coding sequence of SEQ ID NO:1397 shown in Figure 1397.

Figure 1399 shows a nucleotide sequence (SEQ ID NO:1399) of a native sequence PRO38355 cDNA, wherein SEQ ID NO:1399 is a clone designated herein as "DNA327920".

30       Figure 1400 shows the amino acid sequence (SEQ ID NO:1400) derived from the coding sequence of SEQ ID NO:1399 shown in Figure 1399.

Figure 1401 shows a nucleotide sequence (SEQ ID NO:1401) of a native sequence PRO83856 cDNA, wherein SEQ ID NO:1401 is a clone designated herein as "DNA327921".

Figure 1402 shows the amino acid sequence (SEQ ID NO:1402) derived from the coding sequence of SEQ ID NO:1401 shown in Figure 1401.

35       Figure 1403 shows a nucleotide sequence (SEQ ID NO:1403) of a native sequence PRO83857 cDNA, wherein SEQ ID NO:1403 is a clone designated herein as "DNA327922".

Figure 1404 shows the amino acid sequence (SEQ ID NO:1404) derived from the coding sequence of SEQ ID NO:1403 shown in Figure 1403.

40       Figure 1405 shows a nucleotide sequence (SEQ ID NO:1405) of a native sequence PRO6092 cDNA, wherein SEQ ID NO:1405 is a clone designated herein as "DNA327923".

Figure 1406 shows the amino acid sequence (SEQ ID NO:1406) derived from the coding sequence of SEQ ID NO:1405 shown in Figure 1405.

Figure 1407 shows a nucleotide sequence (SEQ ID NO:1407) of a native sequence PRO61855 cDNA, wherein SEQ ID NO:1407 is a clone designated herein as "DNA273901".

5        Figure 1408 shows the amino acid sequence (SEQ ID NO:1408) derived from the coding sequence of SEQ ID NO:1407 shown in Figure 1407.

Figure 1409 shows a nucleotide sequence (SEQ ID NO:1409) of a native sequence PRO12205 cDNA, wherein SEQ ID NO:1409 is a clone designated herein as "DNA151848".

10       Figure 1410 shows the amino acid sequence (SEQ ID NO:1410) derived from the coding sequence of SEQ ID NO:1409 shown in Figure 1409.

Figure 1411 shows a nucleotide sequence (SEQ ID NO:1411) of a native sequence PRO58388 cDNA, wherein SEQ ID NO:1411 is a clone designated herein as "DNA269992".

Figure 1412 shows the amino acid sequence (SEQ ID NO:1412) derived from the coding sequence of SEQ ID NO:1411 shown in Figure 1411.

15       Figure 1413 shows a nucleotide sequence (SEQ ID NO:1413) of a native sequence PRO83858 cDNA, wherein SEQ ID NO:1413 is a clone designated herein as "DNA327924".

Figure 1414 shows the amino acid sequence (SEQ ID NO:1414) derived from the coding sequence of SEQ ID NO:1413 shown in Figure 1413.

20       Figure 1415 shows a nucleotide sequence (SEQ ID NO:1415) of a native sequence PRO83859 cDNA, wherein SEQ ID NO:1415 is a clone designated herein as "DNA327925".

Figure 1416 shows the amino acid sequence (SEQ ID NO:1416) derived from the coding sequence of SEQ ID NO:1415 shown in Figure 1415.

Figure 1417 shows a nucleotide sequence (SEQ ID NO:1417) of a native sequence PRO83860 cDNA, wherein SEQ ID NO:1417 is a clone designated herein as "DNA327926".

25       Figure 1418 shows the amino acid sequence (SEQ ID NO:1418) derived from the coding sequence of SEQ ID NO:1417 shown in Figure 1417.

Figure 1419 shows a nucleotide sequence (SEQ ID NO:1419) of a native sequence PRO57311 cDNA, wherein SEQ ID NO:1419 is a clone designated herein as "DNA327927".

30       Figure 1420 shows the amino acid sequence (SEQ ID NO:1420) derived from the coding sequence of SEQ ID NO:1419 shown in Figure 1419.

Figure 1421 shows a nucleotide sequence (SEQ ID NO:1421) of a native sequence PRO1082 cDNA, wherein SEQ ID NO:1421 is a clone designated herein as "DNA327928".

Figure 1422 shows the amino acid sequence (SEQ ID NO:1422) derived from the coding sequence of SEQ ID NO:1421 shown in Figure 1421.

35       Figure 1423 shows a nucleotide sequence (SEQ ID NO:1423) of a native sequence cDNA, wherein SEQ ID NO:1423 is a clone designated herein as "DNA195869".

Figure 1424 shows a nucleotide sequence (SEQ ID NO:1424) of a native sequence PRO83861 cDNA, wherein SEQ ID NO:1424 is a clone designated herein as "DNA327929".

40       Figure 1425 shows the amino acid sequence (SEQ ID NO:1425) derived from the coding sequence of SEQ ID NO:1424 shown in Figure 1424.

Figure 1426 shows a nucleotide sequence (SEQ ID NO:1426) of a native sequence PRO83862 cDNA, wherein SEQ ID NO:1426 is a clone designated herein as "DNA327930".

Figure 1427 shows the amino acid sequence (SEQ ID NO:1427) derived from the coding sequence of SEQ ID NO:1426 shown in Figure 1426.

5        Figure 1428 shows a nucleotide sequence (SEQ ID NO:1428) of a native sequence PRO83863 cDNA, wherein SEQ ID NO:1428 is a clone designated herein as "DNA327931".

Figure 1429 shows the amino acid sequence (SEQ ID NO:1429) derived from the coding sequence of SEQ ID NO:1428 shown in Figure 1428.

10       Figure 1430 shows a nucleotide sequence (SEQ ID NO:1430) of a native sequence cDNA, wherein SEQ ID NO:1430 is a clone designated herein as "DNA273119".

Figure 1431 shows a nucleotide sequence (SEQ ID NO:1431) of a native sequence PRO83864 cDNA, wherein SEQ ID NO:1431 is a clone designated herein as "DNA327932".

Figure 1432 shows the amino acid sequence (SEQ ID NO:1432) derived from the coding sequence of SEQ ID NO:1431 shown in Figure 1431.

15       Figure 1433 shows a nucleotide sequence (SEQ ID NO:1433) of a native sequence PRO62262 cDNA, wherein SEQ ID NO:1433 is a clone designated herein as "DNA274348".

Figure 1434 shows the amino acid sequence (SEQ ID NO:1434) derived from the coding sequence of SEQ ID NO:1433 shown in Figure 1433.

20       Figure 1435 shows a nucleotide sequence (SEQ ID NO:1435) of a native sequence PRO83865 cDNA, wherein SEQ ID NO:1435 is a clone designated herein as "DNA327933".

Figure 1436 shows the amino acid sequence (SEQ ID NO:1436) derived from the coding sequence of SEQ ID NO:1435 shown in Figure 1435.

Figure 1437 shows a nucleotide sequence (SEQ ID NO:1437) of a native sequence PRO4342 cDNA, wherein SEQ ID NO:1437 is a clone designated herein as "DNA327934".

25       Figure 1438 shows the amino acid sequence (SEQ ID NO:1438) derived from the coding sequence of SEQ ID NO:1437 shown in Figure 1437.

Figure 1439 shows a nucleotide sequence (SEQ ID NO:1439) of a native sequence PRO1314 cDNA, wherein SEQ ID NO:1439 is a clone designated herein as "DNA324364".

30       Figure 1440 shows the amino acid sequence (SEQ ID NO:1440) derived from the coding sequence of SEQ ID NO:1439 shown in Figure 1439.

Figure 1441 shows a nucleotide sequence (SEQ ID NO:1441) of a native sequence PRO83866 cDNA, wherein SEQ ID NO:1441 is a clone designated herein as "DNA327935".

Figure 1442 shows the amino acid sequence (SEQ ID NO:1442) derived from the coding sequence of SEQ ID NO:1441 shown in Figure 1441.

35       Figure 1443 shows a nucleotide sequence (SEQ ID NO:1443) of a native sequence PRO718 cDNA, wherein SEQ ID NO:1443 is a clone designated herein as "DNA327936".

Figure 1444 shows the amino acid sequence (SEQ ID NO:1444) derived from the coding sequence of SEQ ID NO:1443 shown in Figure 1443.

40       Figure 1445 shows a nucleotide sequence (SEQ ID NO:1445) of a native sequence PRO83867 cDNA, wherein SEQ ID NO:1445 is a clone designated herein as "DNA327937".

Figure 1446 shows the amino acid sequence (SEQ ID NO:1446) derived from the coding sequence of SEQ ID NO:1445 shown in Figure 1445.

Figure 1447 shows a nucleotide sequence (SEQ ID NO:1447) of a native sequence PRO11577 cDNA, wherein SEQ ID NO:1447 is a clone designated herein as "DNA150654".

5        Figure 1448 shows the amino acid sequence (SEQ ID NO:1448) derived from the coding sequence of SEQ ID NO:1447 shown in Figure 1447.

Figure 1449 shows a nucleotide sequence (SEQ ID NO:1449) of a native sequence PRO83868 cDNA, wherein SEQ ID NO:1449 is a clone designated herein as "DNA327938".

10       Figure 1450 shows the amino acid sequence (SEQ ID NO:1450) derived from the coding sequence of SEQ ID NO:1449 shown in Figure 1449.

Figure 1451 shows a nucleotide sequence (SEQ ID NO:1451) of a native sequence PRO83869 cDNA, wherein SEQ ID NO:1451 is a clone designated herein as "DNA327939".

Figure 1452 shows the amino acid sequence (SEQ ID NO:1452) derived from the coding sequence of SEQ ID NO:1451 shown in Figure 1451.

15       Figure 1453 shows a nucleotide sequence (SEQ ID NO:1453) of a native sequence PRO50262 cDNA, wherein SEQ ID NO:1453 is a clone designated herein as "DNA255183".

Figure 1454 shows the amino acid sequence (SEQ ID NO:1454) derived from the coding sequence of SEQ ID NO:1453 shown in Figure 1453.

20       Figure 1455 shows a nucleotide sequence (SEQ ID NO:1455) of a native sequence PRO1375 cDNA, wherein SEQ ID NO:1455 is a clone designated herein as "DNA327940".

Figure 1456 shows the amino acid sequence (SEQ ID NO:1456) derived from the coding sequence of SEQ ID NO:1455 shown in Figure 1455.

Figure 1457 shows a nucleotide sequence (SEQ ID NO:1457) of a native sequence PRO944 cDNA, wherein SEQ ID NO:1457 is a clone designated herein as "DNA327941".

25       Figure 1458 shows the amino acid sequence (SEQ ID NO:1458) derived from the coding sequence of SEQ ID NO:1457 shown in Figure 1457.

Figure 1459 shows a nucleotide sequence (SEQ ID NO:1459) of a native sequence PRO83870 cDNA, wherein SEQ ID NO:1459 is a clone designated herein as "DNA327942".

30       Figure 1460 shows the amino acid sequence (SEQ ID NO:1460) derived from the coding sequence of SEQ ID NO:1459 shown in Figure 1459.

Figure 1461 shows a nucleotide sequence (SEQ ID NO:1461) of a native sequence PRO865 cDNA, wherein SEQ ID NO:1461 is a clone designated herein as "DNA327943".

Figure 1462 shows the amino acid sequence (SEQ ID NO:1462) derived from the coding sequence of SEQ ID NO:1461 shown in Figure 1461.

35       Figure 1463 shows a nucleotide sequence (SEQ ID NO:1463) of a native sequence PRO7433 cDNA, wherein SEQ ID NO:1463 is a clone designated herein as "DNA327944".

Figure 1464 shows the amino acid sequence (SEQ ID NO:1464) derived from the coding sequence of SEQ ID NO:1463 shown in Figure .

40       Figure 1465 shows a nucleotide sequence (SEQ ID NO:1465) of a native sequence PRO82384 cDNA, wherein SEQ ID NO:1465 is a clone designated herein as "DNA325936".

Figure 1466 shows the amino acid sequence (SEQ ID NO:1466) derived from the coding sequence of SEQ ID NO:1465 shown in Figure 1465.

Figure 1467 shows a nucleotide sequence (SEQ ID NO:1467) of a native sequence PRO83871 cDNA, wherein SEQ ID NO:1467 is a clone designated herein as "DNA327945".

5        Figure 1468 shows the amino acid sequence (SEQ ID NO:1468) derived from the coding sequence of SEQ ID NO:1467 shown in Figure 1467.

Figure 1469 shows a nucleotide sequence (SEQ ID NO:1469) of a native sequence PRO49401 cDNA, wherein SEQ ID NO:1469 is a clone designated herein as "DNA254290".

10       Figure 1470 shows the amino acid sequence (SEQ ID NO:1470) derived from the coding sequence of SEQ ID NO:1469 shown in Figure 1469.

Figure 1471 shows a nucleotide sequence (SEQ ID NO:1471) of a native sequence PRO83872 cDNA, wherein SEQ ID NO:1471 is a clone designated herein as "DNA327946".

Figure 1472 shows the amino acid sequence (SEQ ID NO:1472) derived from the coding sequence of SEQ ID NO:1471 shown in Figure 1471.

15       Figure 1473 shows a nucleotide sequence (SEQ ID NO:1473) of a native sequence PRO83873 cDNA, wherein SEQ ID NO:1473 is a clone designated herein as "DNA327947".

Figure 1474 shows the amino acid sequence (SEQ ID NO:1474) derived from the coding sequence of SEQ ID NO:1473 shown in Figure 1473.

20       Figure 1475 shows a nucleotide sequence (SEQ ID NO:1475) of a native sequence PRO10928 cDNA, wherein SEQ ID NO:1475 is a clone designated herein as "DNA152786".

Figure 1476 shows the amino acid sequence (SEQ ID NO:1476) derived from the coding sequence of SEQ ID NO:1475 shown in Figure 1475.

Figure 1477 shows a nucleotide sequence (SEQ ID NO:1477) of a native sequence PRO81339 cDNA, wherein SEQ ID NO:1477 is a clone designated herein as "DNA324707".

25       Figure 1478 shows the amino acid sequence (SEQ ID NO:1478) derived from the coding sequence of SEQ ID NO:1477 shown in Figure 1477.

Figure 1479 shows a nucleotide sequence (SEQ ID NO:1479) of a native sequence PRO69660 cDNA, wherein SEQ ID NO:1479 is a clone designated herein as "DNA327948".

30       Figure 1480 shows the amino acid sequence (SEQ ID NO:1480) derived from the coding sequence of SEQ ID NO:1479 shown in Figure 1479.

Figure 1481 shows a nucleotide sequence (SEQ ID NO:1481) of a native sequence PRO83874 cDNA, wherein SEQ ID NO:1481 is a clone designated herein as "DNA327949".

Figure 1482 shows the amino acid sequence (SEQ ID NO:1482) derived from the coding sequence of SEQ ID NO:1481 shown in Figure 1481.

35       Figure 1483 shows a nucleotide sequence (SEQ ID NO:1483) of a native sequence PRO83875 cDNA, wherein SEQ ID NO:1483 is a clone designated herein as "DNA327950".

Figure 1484 shows the amino acid sequence (SEQ ID NO:1484) derived from the coding sequence of SEQ ID NO:1483 shown in Figure 1483.

40       Figure 1485 shows a nucleotide sequence (SEQ ID NO:1485) of a native sequence PRO83876 cDNA, wherein SEQ ID NO:1485 is a clone designated herein as "DNA327951".



Figure 1486 shows the amino acid sequence (SEQ ID NO:1486) derived from the coding sequence of SEQ ID NO:1485 shown in Figure 1485.

Figure 1487 shows a nucleotide sequence (SEQ ID NO:1487) of a native sequence PRO83877 cDNA, wherein SEQ ID NO:1487 is a clone designated herein as "DNA327952".

5 Figure 1488 shows the amino acid sequence (SEQ ID NO:1488) derived from the coding sequence of SEQ ID NO:1487 shown in Figure .

Figure 1489 shows a nucleotide sequence (SEQ ID NO:1489) of a native sequence PRO83878 cDNA, wherein SEQ ID NO:1489 is a clone designated herein as "DNA327953".

10 Figure 1490 shows the amino acid sequence (SEQ ID NO:1490) derived from the coding sequence of SEQ ID NO:1489 shown in Figure 1489.

Figure 1491 shows a nucleotide sequence (SEQ ID NO:1491) of a native sequence PRO52040 cDNA, wherein SEQ ID NO:1491 is a clone designated herein as "DNA257461".

Figure 1492 shows the amino acid sequence (SEQ ID NO:1492) derived from the coding sequence of SEQ ID NO:1491 shown in Figure 1491.

15 Figure 1493 shows a nucleotide sequence (SEQ ID NO:1493) of a native sequence PRO83879 cDNA, wherein SEQ ID NO:1493 is a clone designated herein as "DNA327954".

Figure 1494 shows the amino acid sequence (SEQ ID NO:1494) derived from the coding sequence of SEQ ID NO:1493 shown in Figure 1493.

20 Figure 1495 shows a nucleotide sequence (SEQ ID NO:1495) of a native sequence PRO83880 cDNA, wherein SEQ ID NO:1495 is a clone designated herein as "DNA327955".

Figure 1496 shows the amino acid sequence (SEQ ID NO:1496) derived from the coding sequence of SEQ ID NO:1495 shown in Figure 1495.

Figure 1497 shows a nucleotide sequence (SEQ ID NO:1497) of a native sequence PRO83881 cDNA, wherein SEQ ID NO:1497 is a clone designated herein as "DNA327956".

25 Figure 1498 shows the amino acid sequence (SEQ ID NO:1498) derived from the coding sequence of SEQ ID NO:1497 shown in Figure 1497.

Figure 1499 shows a nucleotide sequence (SEQ ID NO:1499) of a native sequence PRO83882 cDNA, wherein SEQ ID NO:1499 is a clone designated herein as "DNA327957".

30 Figure 1500 shows the amino acid sequence (SEQ ID NO:1500) derived from the coding sequence of SEQ ID NO:1499 shown in Figure 1499.

Figure 1501 shows a nucleotide sequence (SEQ ID NO:1501) of a native sequence PRO82861 cDNA, wherein SEQ ID NO:1501 is a clone designated herein as "DNA326483".

Figure 1502 shows the amino acid sequence (SEQ ID NO:1502) derived from the coding sequence of SEQ ID NO:1501 shown in Figure 1501.

35 Figure 1503 shows a nucleotide sequence (SEQ ID NO:1503) of a native sequence PRO50738 cDNA, wherein SEQ ID NO:1503 is a clone designated herein as "DNA255676".

Figure 1504 shows the amino acid sequence (SEQ ID NO:1504) derived from the coding sequence of SEQ ID NO:1503 shown in Figure 1503.

40 Figure 1505 shows a nucleotide sequence (SEQ ID NO:1505) of a native sequence PRO61417 cDNA, wherein SEQ ID NO:1505 is a clone designated herein as "DNA273418".

Figure 1506 shows the amino acid sequence (SEQ ID NO:1506) derived from the coding sequence of SEQ ID NO:1505 shown in Figure 1505.

Figure 1507 shows a nucleotide sequence (SEQ ID NO:1507) of a native sequence PRO23554 cDNA, wherein SEQ ID NO:1507 is a clone designated herein as "DNA327958".

5        Figure 1508 shows the amino acid sequence (SEQ ID NO:1508) derived from the coding sequence of SEQ ID NO:1507 shown in Figure 1507.

Figure 1509 shows a nucleotide sequence (SEQ ID NO:1509) of a native sequence PRO83883 cDNA, wherein SEQ ID NO:1509 is a clone designated herein as "DNA327959".

10       Figure 1510 shows the amino acid sequence (SEQ ID NO:1510) derived from the coding sequence of SEQ ID NO:1509 shown in Figure 1509.

Figure 1511 shows a nucleotide sequence (SEQ ID NO:1511) of a native sequence PRO52449 cDNA, wherein SEQ ID NO:1511 is a clone designated herein as "DNA257916".

Figure 1512 shows the amino acid sequence (SEQ ID NO:1512) derived from the coding sequence of SEQ ID NO:1511 shown in Figure 1511.

15       Figure 1513 shows a nucleotide sequence (SEQ ID NO:1513) of a native sequence PRO83884 cDNA, wherein SEQ ID NO:1513 is a clone designated herein as "DNA327960".

Figure 1514 shows the amino acid sequence (SEQ ID NO:1514) derived from the coding sequence of SEQ ID NO:1513 shown in Figure .

20       Figure 1515 shows a nucleotide sequence (SEQ ID NO:1515) of a native sequence PRO83885 cDNA, wherein SEQ ID NO:1515 is a clone designated herein as "DNA327961".

Figure 1516 shows the amino acid sequence (SEQ ID NO:1516) derived from the coding sequence of SEQ ID NO:1515 shown in Figure 1515.

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Figure 1517 shows a nucleotide sequence (SEQ ID NO:1517) of a native sequence PRO54660 cDNA, wherein SEQ ID NO:1517 is a clone designated herein as "DNA327962".

25       Figure 1518 shows the amino acid sequence (SEQ ID NO:1518) derived from the coding sequence of SEQ ID NO:1517 shown in Figure 1517.

Figure 1519 shows a nucleotide sequence (SEQ ID NO:1519) of a native sequence PRO83886 cDNA, wherein SEQ ID NO:1519 is a clone designated herein as "DNA327963".

30       Figure 1520 shows the amino acid sequence (SEQ ID NO:1520) derived from the coding sequence of SEQ ID NO:1519 shown in Figure 1519.

Figure 1521 shows a nucleotide sequence (SEQ ID NO:1521) of a native sequence PRO83887 cDNA, wherein SEQ ID NO:1521 is a clone designated herein as "DNA327964".

Figure 1522 shows the amino acid sequence (SEQ ID NO:1522) derived from the coding sequence of SEQ ID NO:1521 shown in Figure 1521.

35       Figure 1523 shows a nucleotide sequence (SEQ ID NO:1523) of a native sequence PRO83888 cDNA, wherein SEQ ID NO:1523 is a clone designated herein as "DNA327965".

Figure 1524 shows the amino acid sequence (SEQ ID NO:1524) derived from the coding sequence of SEQ ID NO:1523 shown in Figure 1523.

40       Figure 1525 shows a nucleotide sequence (SEQ ID NO:1525) of a native sequence PRO83889 cDNA, wherein SEQ ID NO:1525 is a clone designated herein as "DNA327966".

Figure 1526 shows the amino acid sequence (SEQ ID NO:1526) derived from the coding sequence of SEQ ID NO:1525 shown in Figure 1525.

Figure 1527 shows a nucleotide sequence (SEQ ID NO:1527) of a native sequence PRO1065 cDNA, wherein SEQ ID NO:1527 is a clone designated herein as "DNA327200".

5 Figure 1528 shows the amino acid sequence (SEQ ID NO:1528) derived from the coding sequence of SEQ ID NO:1527 shown in Figure 1527.

Figure 1529 shows a nucleotide sequence (SEQ ID NO:1529) of a native sequence PRO83890 cDNA, wherein SEQ ID NO:1529 is a clone designated herein as "DNA327967".

10 Figure 1530 shows the amino acid sequence (SEQ ID NO:1530) derived from the coding sequence of SEQ ID NO:1529 shown in Figure 1529.

Figure 1531 shows a nucleotide sequence (SEQ ID NO:1531) of a native sequence PRO83891 cDNA, wherein SEQ ID NO:1531 is a clone designated herein as "DNA327968".

Figure 1532 shows the amino acid sequence (SEQ ID NO:1532) derived from the coding sequence of SEQ ID NO:1531 shown in Figure 1531.

15 Figure 1533 shows a nucleotide sequence (SEQ ID NO:1533) of a native sequence PRO301 cDNA, wherein SEQ ID NO:1533 is a clone designated herein as "DNA327969".

Figure 1534 shows the amino acid sequence (SEQ ID NO:1534) derived from the coding sequence of SEQ ID NO:1533 shown in Figure 1533.

20 Figure 1535 shows a nucleotide sequence (SEQ ID NO:1535) of a native sequence PRO83473 cDNA, wherein SEQ ID NO:1535 is a clone designated herein as "DNA327197".

Figure 1536 shows the amino acid sequence (SEQ ID NO:1536) derived from the coding sequence of SEQ ID NO:1535 shown in Figure 1535.

Figure 1537 shows a nucleotide sequence (SEQ ID NO:1537) of a native sequence PRO83892 cDNA, wherein SEQ ID NO:1537 is a clone designated herein as "DNA327970".

25 Figure 1538 shows the amino acid sequence (SEQ ID NO:1538) derived from the coding sequence of SEQ ID NO:1537 shown in Figure 1537.

Figure 1539 shows a nucleotide sequence (SEQ ID NO:1539) of a native sequence PRO83893 cDNA, wherein SEQ ID NO:1539 is a clone designated herein as "DNA327971".

30 Figure 1540 shows the amino acid sequence (SEQ ID NO:1540) derived from the coding sequence of SEQ ID NO:1539 shown in Figure 1539.

Figure 1541 shows a nucleotide sequence (SEQ ID NO:1541) of a native sequence PRO83474 cDNA, wherein SEQ ID NO:1541 is a clone designated herein as "DNA327198".

Figure 1542 shows the amino acid sequence (SEQ ID NO:1542) derived from the coding sequence of SEQ ID NO:1541 shown in Figure 1541.

35 Figure 1543 shows a nucleotide sequence (SEQ ID NO:1543) of a native sequence PRO83894 cDNA, wherein SEQ ID NO:1543 is a clone designated herein as "DNA327972".

Figure 1544 shows the amino acid sequence (SEQ ID NO:1544) derived from the coding sequence of SEQ ID NO:1543 shown in Figure 1543.

40 Figure 1545 shows a nucleotide sequence (SEQ ID NO:1545) of a native sequence PRO83895 cDNA, wherein SEQ ID NO:1545 is a clone designated herein as "DNA327973".

Figure 1546 shows the amino acid sequence (SEQ ID NO:1546) derived from the coding sequence of SEQ ID NO:1545 shown in Figure 1545.

Figure 1547 shows a nucleotide sequence (SEQ ID NO:1547) of a native sequence PRO83896 cDNA, wherein SEQ ID NO:1547 is a clone designated herein as "DNA327974".

5 Figure 1548 shows the amino acid sequence (SEQ ID NO:1548) derived from the coding sequence of SEQ ID NO:1547 shown in Figure 1547.

Figure 1549 shows a nucleotide sequence (SEQ ID NO:1549) of a native sequence PRO83897 cDNA, wherein SEQ ID NO:1549 is a clone designated herein as "DNA327975".

10 Figure 1550 shows the amino acid sequence (SEQ ID NO:1550) derived from the coding sequence of SEQ ID NO:1549 shown in Figure 1549.

Figure 1551 shows a nucleotide sequence (SEQ ID NO:1551) of a native sequence PRO69574 cDNA, wherein SEQ ID NO:1551 is a clone designated herein as "DNA327976".

Figure 1552 shows the amino acid sequence (SEQ ID NO:1552) derived from the coding sequence of SEQ ID NO:1521 shown in Figure 1521.

15 Figure 1553 shows a nucleotide sequence (SEQ ID NO:1553) of a native sequence PRO83898 cDNA, wherein SEQ ID NO:1553 is a clone designated herein as "DNA327977".

Figure 1554 shows the amino acid sequence (SEQ ID NO:1554) derived from the coding sequence of SEQ ID NO:1553 shown in Figure 1553.

20 Figure 1555 shows a nucleotide sequence (SEQ ID NO:1555) of a native sequence PRO83899 cDNA, wherein SEQ ID NO:1555 is a clone designated herein as "DNA327978".

Figure 1556 shows the amino acid sequence (SEQ ID NO:1556) derived from the coding sequence of SEQ ID NO:1555 shown in Figure 1555.

Figure 1557 shows a nucleotide sequence (SEQ ID NO:1557) of a native sequence PRO82633 cDNA, wherein SEQ ID NO:1557 is a clone designated herein as "DNA327979".

25 Figure 1558 shows the amino acid sequence (SEQ ID NO:1558) derived from the coding sequence of SEQ ID NO:1557 shown in Figure 1557.

Figure 1559 shows a nucleotide sequence (SEQ ID NO:1559) of a native sequence PRO83900 cDNA, wherein SEQ ID NO:1559 is a clone designated herein as "DNA327980".

30 Figure 1560 shows the amino acid sequence (SEQ ID NO:1560) derived from the coding sequence of SEQ ID NO:1559 shown in Figure 1559.

Figure 1561 shows a nucleotide sequence (SEQ ID NO:1561) of a native sequence PRO83901 cDNA, wherein SEQ ID NO:1561 is a clone designated herein as "DNA327981".

Figure 1562 shows the amino acid sequence (SEQ ID NO:1562) derived from the coding sequence of SEQ ID NO:1561 shown in Figure 1561.

35 Figure 1563 shows a nucleotide sequence (SEQ ID NO:1563) of a native sequence PRO83902 cDNA, wherein SEQ ID NO:1563 is a clone designated herein as "DNA327982".

Figure 1564 shows the amino acid sequence (SEQ ID NO:1564) derived from the coding sequence of SEQ ID NO:1563 shown in Figure 1563.

40 Figure 1565 shows a nucleotide sequence (SEQ ID NO:1565) of a native sequence PRO83903 cDNA, wherein SEQ ID NO:1565 is a clone designated herein as "DNA327983".

Figure 1566 shows the amino acid sequence (SEQ ID NO:1566) derived from the coding sequence of SEQ ID NO:1565 shown in Figure 1565.

Figure 1567 shows a nucleotide sequence (SEQ ID NO:1567) of a native sequence PRO83904 cDNA, wherein SEQ ID NO:1567 is a clone designated herein as "DNA327984".

5        Figure 1568 shows the amino acid sequence (SEQ ID NO:1568) derived from the coding sequence of SEQ ID NO:1567 shown in Figure 1567.

Figure 1569 shows a nucleotide sequence (SEQ ID NO:1569) of a native sequence PRO23253 cDNA, wherein SEQ ID NO:1569 is a clone designated herein as "DNA169523".

10       Figure 1570 shows the amino acid sequence (SEQ ID NO:1570) derived from the coding sequence of SEQ ID NO:1569 shown in Figure 1569.

Figure 1571 shows a nucleotide sequence (SEQ ID NO:1571) of a native sequence PRO83905 cDNA, wherein SEQ ID NO:1571 is a clone designated herein as "DNA327985".

Figure 1572 shows the amino acid sequence (SEQ ID NO:1572) derived from the coding sequence of SEQ ID NO:1571 shown in Figure 1571.

15       Figure 1573 shows a nucleotide sequence (SEQ ID NO:1573) of a native sequence PRO83906 cDNA, wherein SEQ ID NO:1573 is a clone designated herein as "DNA327986".

Figure 1574 shows the amino acid sequence (SEQ ID NO:1574) derived from the coding sequence of SEQ ID NO:1573 shown in Figure 1573.

20       Figure 1575 shows a nucleotide sequence (SEQ ID NO:1575) of a native sequence PRO83907 cDNA, wherein SEQ ID NO:1575 is a clone designated herein as "DNA327987".

Figure 1576 shows the amino acid sequence (SEQ ID NO:1576) derived from the coding sequence of SEQ ID NO:1575 shown in Figure 1575.

Figure 1577 shows a nucleotide sequence (SEQ ID NO:1577) of a native sequence PRO83908 cDNA, wherein SEQ ID NO:1577 is a clone designated herein as "DNA327988".

25       Figure 1578 shows the amino acid sequence (SEQ ID NO:1578) derived from the coding sequence of SEQ ID NO:1577 shown in Figure 1577.

Figure 1579 shows a nucleotide sequence (SEQ ID NO:1579) of a native sequence PRO83909 cDNA, wherein SEQ ID NO:1579 is a clone designated herein as "DNA327989".

30       Figure 1580 shows the amino acid sequence (SEQ ID NO:1580) derived from the coding sequence of SEQ ID NO:1579 shown in Figure 1579.

Figure 1581 shows a nucleotide sequence (SEQ ID NO:1581) of a native sequence PRO83910 cDNA, wherein SEQ ID NO:1581 is a clone designated herein as "DNA327990".

Figure 1582 shows the amino acid sequence (SEQ ID NO:1582) derived from the coding sequence of SEQ ID NO:1581 shown in Figure 1581.

35       Figure 1583 shows a nucleotide sequence (SEQ ID NO:1583) of a native sequence cDNA, wherein SEQ ID NO:1583 is a clone designated herein as "DNA327991".

Figure 1584 shows a nucleotide sequence (SEQ ID NO:1584) of a native sequence PRO83912 cDNA, wherein SEQ ID NO:1584 is a clone designated herein as "DNA327992".

40       Figure 1585 shows the amino acid sequence (SEQ ID NO:1585) derived from the coding sequence of SEQ ID NO:1584 shown in Figure 1584.

Figure 1586 shows a nucleotide sequence (SEQ ID NO:1586) of a native sequence PRO81138 cDNA, wherein SEQ ID NO:1586 is a clone designated herein as "DNA327993".

Figure 1587 shows the amino acid sequence (SEQ ID NO:1587) derived from the coding sequence of SEQ ID NO:1586 shown in Figure 1586.

5        Figure 1588 shows a nucleotide sequence (SEQ ID NO:1588) of a native sequence cDNA, wherein SEQ ID NO:1588 is a clone designated herein as "DNA327994".

Figure 1589 shows a nucleotide sequence (SEQ ID NO:1589) of a native sequence PRO83914 cDNA, wherein SEQ ID NO:1589 is a clone designated herein as "DNA327995".

10       Figure 1590 shows the amino acid sequence (SEQ ID NO:1590) derived from the coding sequence of SEQ ID NO:1589 shown in Figure 1589.

Figure 1591 shows a nucleotide sequence (SEQ ID NO:1591) of a native sequence PRO83915 cDNA, wherein SEQ ID NO:1591 is a clone designated herein as "DNA327996".

Figure 1592 shows the amino acid sequence (SEQ ID NO:1592) derived from the coding sequence of SEQ ID NO:1591 shown in Figure 1591.

15       Figure 1593 shows a nucleotide sequence (SEQ ID NO:1593) of a native sequence PRO83916 cDNA, wherein SEQ ID NO:1593 is a clone designated herein as "DNA327997".

Figure 1594 shows the amino acid sequence (SEQ ID NO:1594) derived from the coding sequence of SEQ ID NO:1593 shown in Figure 1593.

20       Figure 1595 shows a nucleotide sequence (SEQ ID NO:1595) of a native sequence cDNA, wherein SEQ ID NO:1595 is a clone designated herein as "DNA327998".

Figure 1596 shows a nucleotide sequence (SEQ ID NO:1596) of a native sequence PRO83918 cDNA, wherein SEQ ID NO:1596 is a clone designated herein as "DNA327999".

Figure 1597 shows the amino acid sequence (SEQ ID NO:1597) derived from the coding sequence of SEQ ID NO:1596 shown in Figure 1596.

25       Figure 1598 shows a nucleotide sequence (SEQ ID NO:1598) of a native sequence PRO83919 cDNA, wherein SEQ ID NO:1598 is a clone designated herein as "DNA328000".

Figure 1599 shows the amino acid sequence (SEQ ID NO:1599) derived from the coding sequence of SEQ ID NO:1598 shown in Figure 1598.

30       Figure 1600 shows a nucleotide sequence (SEQ ID NO:1600) of a native sequence PRO83920 cDNA, wherein SEQ ID NO:1600 is a clone designated herein as "DNA328001".

Figure 1601 shows the amino acid sequence (SEQ ID NO:1601) derived from the coding sequence of SEQ ID NO:1600 shown in Figure 1600.

Figure 1602 shows a nucleotide sequence (SEQ ID NO:1602) of a native sequence PRO83921 cDNA, wherein SEQ ID NO:1602 is a clone designated herein as "DNA328002".

35       Figure 1603 shows the amino acid sequence (SEQ ID NO:1603) derived from the coding sequence of SEQ ID NO:1602 shown in Figure 1602.

Figure 1604 shows a nucleotide sequence (SEQ ID NO:1604) of a native sequence PRO83922 cDNA, wherein SEQ ID NO:1604 is a clone designated herein as "DNA328003".

40       Figure 1605 shows the amino acid sequence (SEQ ID NO:1605) derived from the coding sequence of SEQ ID NO:1604 shown in Figure 1604.

Figure 1606 shows a nucleotide sequence (SEQ ID NO:1606) of a native sequence PRO83923 cDNA, wherein SEQ ID NO:1606 is a clone designated herein as "DNA328004".

Figure 1607 shows the amino acid sequence (SEQ ID NO:1607) derived from the coding sequence of SEQ ID NO:1606 shown in Figure 1606.

5        Figure 1608 shows a nucleotide sequence (SEQ ID NO:1608) of a native sequence cDNA, wherein SEQ ID NO:1608 is a clone designated herein as "DNA328005".

Figure 1609 shows a nucleotide sequence (SEQ ID NO:1509) of a native sequence PRO83924 cDNA, wherein SEQ ID NO:1609 is a clone designated herein as "DNA328006".

10       Figure 1610 shows the amino acid sequence (SEQ ID NO:1610) derived from the coding sequence of SEQ ID NO:1609 shown in Figure 1609.

Figure 1611 shows a nucleotide sequence (SEQ ID NO:1611) of a native sequence cDNA, wherein SEQ ID NO:1611 is a clone designated herein as "DNA255056".

Figure 1612 shows a nucleotide sequence (SEQ ID NO:1612) of a native sequence PRO83925 cDNA, wherein SEQ ID NO:1612 is a clone designated herein as "DNA328007".

15       Figure 1613 shows the amino acid sequence (SEQ ID NO:1613) derived from the coding sequence of SEQ ID NO:1612 shown in Figure 1612.

Figure 1614 shows a nucleotide sequence (SEQ ID NO:1614) of a native sequence PRO83926 cDNA, wherein SEQ ID NO:1614 is a clone designated herein as "DNA328008".

20       Figure 1615 shows the amino acid sequence (SEQ ID NO:1615) derived from the coding sequence of SEQ ID NO:1614 shown in Figure 1614.

Figure 1616 shows a nucleotide sequence (SEQ ID NO:1616) of a native sequence PRO83927 cDNA, wherein ~~SEQ ID NO:1616 is a clone designated herein as "DNA328009".~~

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Figure 1617 shows the amino acid sequence (SEQ ID NO:1617) derived from the coding sequence of SEQ ID NO:1616 shown in Figure 1616.

25       Figure 1618 shows a nucleotide sequence (SEQ ID NO:1618) of a native sequence PRO83928 cDNA, wherein SEQ ID NO:1618 is a clone designated herein as "DNA328010".

Figure 1619 shows the amino acid sequence (SEQ ID NO:1619) derived from the coding sequence of SEQ ID NO:1618 shown in Figure 1618.

30       Figure 1620 shows a nucleotide sequence (SEQ ID NO:1620) of a native sequence PRO28545 cDNA, wherein SEQ ID NO:1620 is a clone designated herein as "DNA199088".

Figure 1621 shows the amino acid sequence (SEQ ID NO:1621) derived from the coding sequence of SEQ ID NO:1620 shown in Figure 1620.

Figure 1622 shows a nucleotide sequence (SEQ ID NO:1622) of a native sequence PRO70021 cDNA, wherein SEQ ID NO:1622 is a clone designated herein as "DNA288261".

35       Figure 1623 shows the amino acid sequence (SEQ ID NO:1623) derived from the coding sequence of SEQ ID NO:1622 shown in Figure 1622.

Figure 1624 shows a nucleotide sequence (SEQ ID NO:1624) of a native sequence PRO83929 cDNA, wherein SEQ ID NO:1624 is a clone designated herein as "DNA328011".

40       Figure 1625 shows the amino acid sequence (SEQ ID NO:1625) derived from the coding sequence of SEQ ID NO:1624 shown in Figure 1624.

Figure 1626 shows a nucleotide sequence (SEQ ID NO:1626) of a native sequence PRO83930 cDNA, wherein SEQ ID NO:1626 is a clone designated herein as "DNA328012".

Figure 1627 shows the amino acid sequence (SEQ ID NO:1627) derived from the coding sequence of SEQ ID NO:1626 shown in Figure 1626.

5        Figure 1628 shows a nucleotide sequence (SEQ ID NO:1628) of a native sequence PRO83931 cDNA, wherein SEQ ID NO:1628 is a clone designated herein as "DNA328013".

Figure 1629 shows the amino acid sequence (SEQ ID NO:1629) derived from the coding sequence of SEQ ID NO:1628 shown in Figure 1628.

10       Figure 1630 shows a nucleotide sequence (SEQ ID NO:1630) of a native sequence PRO83932 cDNA, wherein SEQ ID NO:1630 is a clone designated herein as "DNA328014".

Figure 1631 shows the amino acid sequence (SEQ ID NO:1631) derived from the coding sequence of SEQ ID NO:1630 shown in Figure 1630.

Figure 1632 shows a nucleotide sequence (SEQ ID NO:1632) of a native sequence PRO50889 cDNA, wherein SEQ ID NO:1632 is a clone designated herein as "DNA255834".

15       Figure 1633 shows the amino acid sequence (SEQ ID NO:1633) derived from the coding sequence of SEQ ID NO:1632 shown in Figure 1632.

Figure 1634 shows a nucleotide sequence (SEQ ID NO:1634) of a native sequence PRO865 cDNA, wherein SEQ ID NO:1634 is a clone designated herein as "DNA260947".

20       Figure 1635 shows the amino acid sequence (SEQ ID NO:1635) derived from the coding sequence of SEQ ID NO:1634 shown in Figure 1634.

Figure 1636 shows a nucleotide sequence (SEQ ID NO:1636) of a native sequence PRO83933 cDNA, wherein SEQ ID NO:1636 is a clone designated herein as "DNA328015".

Figure 1637 shows the amino acid sequence (SEQ ID NO:1637) derived from the coding sequence of SEQ ID NO:1636 shown in Figure 1636.

25       Figure 1638 shows a nucleotide sequence (SEQ ID NO:1638) of a native sequence PRO83934 cDNA, wherein SEQ ID NO:1638 is a clone designated herein as "DNA328016".

Figure 1639 shows the amino acid sequence (SEQ ID NO:1639) derived from the coding sequence of SEQ ID NO:1638 shown in Figure 1638.

30       Figure 1640 shows a nucleotide sequence (SEQ ID NO:1640) of a native sequence PRO83935 cDNA, wherein SEQ ID NO:1640 is a clone designated herein as "DNA328017".

Figure 1641 shows the amino acid sequence (SEQ ID NO:1641) derived from the coding sequence of SEQ ID NO:1640 shown in Figure 1640.

Figure 1642 shows a nucleotide sequence (SEQ ID NO:1642) of a native sequence PRO83936 cDNA, wherein SEQ ID NO:1642 is a clone designated herein as "DNA328018".

35       Figure 1643 shows the amino acid sequence (SEQ ID NO:1643) derived from the coding sequence of SEQ ID NO:1642 shown in Figure 1642.

Figure 1644 shows a nucleotide sequence (SEQ ID NO:1644) of a native sequence PRO83937 cDNA, wherein SEQ ID NO:1644 is a clone designated herein as "DNA328019".

40       Figure 1645 shows the amino acid sequence (SEQ ID NO:1645) derived from the coding sequence of SEQ ID NO:1645 shown in Figure 1643.



Figure 1646 shows a nucleotide sequence (SEQ ID NO:1646) of a native sequence PRO83938 cDNA, wherein SEQ ID NO:1646 is a clone designated herein as "DNA328020".

Figure 1647 shows the amino acid sequence (SEQ ID NO:1647) derived from the coding sequence of SEQ ID NO:1646 shown in Figure 1646.

5        Figure 1648 shows a nucleotide sequence (SEQ ID NO:1648) of a native sequence cDNA, wherein SEQ ID NO:1648 is a clone designated herein as "DNA268880".

Figure 1649 shows a nucleotide sequence (SEQ ID NO:1649) of a native sequence PRO1190 cDNA, wherein SEQ ID NO:1649 is a clone designated herein as "DNA59586".

10       Figure 1650 shows the amino acid sequence (SEQ ID NO:1650) derived from the coding sequence of SEQ ID NO:1649 shown in Figure 1649.

Figure 1651 shows a nucleotide sequence (SEQ ID NO:1651) of a native sequence cDNA, wherein SEQ ID NO:1651 is a clone designated herein as "DNA328021".

Figure 1652 shows a nucleotide sequence (SEQ ID NO:1652) of a native sequence cDNA, wherein SEQ ID NO:1652 is a clone designated herein as "DNA328022".

15       Figure 1653 shows a nucleotide sequence (SEQ ID NO:1653) of a native sequence PRO61223 cDNA, wherein SEQ ID NO:1653 is a clone designated herein as "DNA328023".

Figure 1654 shows the amino acid sequence (SEQ ID NO:1654) derived from the coding sequence of SEQ ID NO:1653 shown in Figure 1653.

20       Figure 1655 shows a nucleotide sequence (SEQ ID NO:1655) of a native sequence PRO83941 cDNA, wherein SEQ ID NO:1655 is a clone designated herein as "DNA328024".

Figure 1656 shows the amino acid sequence (SEQ ID NO:1656) derived from the coding sequence of SEQ ID NO:1655 shown in Figure 1655.

Figure 1657 shows a nucleotide sequence (SEQ ID NO:1657) of a native sequence PRO83942 cDNA, wherein SEQ ID NO:1657 is a clone designated herein as "DNA328025".

25       Figure 1658 shows the amino acid sequence (SEQ ID NO:1658) derived from the coding sequence of SEQ ID NO:1657 shown in Figure 1657.

Figure 1659 shows a nucleotide sequence (SEQ ID NO:1659) of a native sequence PRO83943 cDNA, wherein SEQ ID NO:1659 is a clone designated herein as "DNA328026".

30       Figure 1660 shows the amino acid sequence (SEQ ID NO:1660) derived from the coding sequence of SEQ ID NO:1659 shown in Figure 1659.

Figure 1661 shows a nucleotide sequence (SEQ ID NO:1661) of a native sequence PRO23314 cDNA, wherein SEQ ID NO:1661 is a clone designated herein as "DNA193896".

Figure 1662 shows the amino acid sequence (SEQ ID NO:1662) derived from the coding sequence of SEQ ID NO:1661 shown in Figure 1661.

35       Figure 1663 shows a nucleotide sequence (SEQ ID NO:1663) of a native sequence PRO83944 cDNA, wherein SEQ ID NO:1663 is a clone designated herein as "DNA328027".

Figure 1664 shows the amino acid sequence (SEQ ID NO:1664) derived from the coding sequence of SEQ ID NO:1663 shown in Figure 1663.

40       Figure 1665 shows a nucleotide sequence (SEQ ID NO:1665) of a native sequence PRO83945 cDNA, wherein SEQ ID NO:1665 is a clone designated herein as "DNA328028".

Figure 1666 shows the amino acid sequence (SEQ ID NO:1666) derived from the coding sequence of SEQ ID NO:1665 shown in Figure 1665.

Figure 1667 shows a nucleotide sequence (SEQ ID NO:1667) of a native sequence PRO83946 cDNA, wherein SEQ ID NO:1667 is a clone designated herein as "DNA328029".

5        Figure 1668 shows the amino acid sequence (SEQ ID NO:1668) derived from the coding sequence of SEQ ID NO:1667 shown in Figure 1667.

Figure 1669 shows a nucleotide sequence (SEQ ID NO:1669) of a native sequence PRO4977 cDNA, wherein SEQ ID NO:1669 is a clone designated herein as "DNA62849".

10       Figure 1670 shows the amino acid sequence (SEQ ID NO:1670) derived from the coding sequence of SEQ ID NO:1669 shown in Figure 1669.

Figure 1671 shows a nucleotide sequence (SEQ ID NO:1671) of a native sequence PRO83947 cDNA, wherein SEQ ID NO:1671 is a clone designated herein as "DNA328030".

Figure 1672 shows the amino acid sequence (SEQ ID NO:1672) derived from the coding sequence of SEQ ID NO:1671 shown in Figure 1671.

15       Figure 1673 shows a nucleotide sequence (SEQ ID NO:1673) of a native sequence PRO83948 cDNA, wherein SEQ ID NO:1673 is a clone designated herein as "DNA328031".

Figure 1674 shows the amino acid sequence (SEQ ID NO:1674) derived from the coding sequence of SEQ ID NO:1673 shown in Figure 1673.

20       Figure 1675 shows a nucleotide sequence (SEQ ID NO:1675) of a native sequence PRO71114 cDNA, wherein SEQ ID NO:1675 is a clone designated herein as "DNA328032".

Figure 1676 shows the amino acid sequence (SEQ ID NO:1676) derived from the coding sequence of SEQ ID NO:1675 shown in Figure 1675.

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Figure 1677 shows a nucleotide sequence (SEQ ID NO:1677) of a native sequence PRO83949 cDNA, wherein SEQ ID NO:1677 is a clone designated herein as "DNA328033".

25       Figure 1678 shows the amino acid sequence (SEQ ID NO:1678) derived from the coding sequence of SEQ ID NO:1677 shown in Figure 1677.

Figure 1679 shows a nucleotide sequence (SEQ ID NO:1679) of a native sequence PRO83950 cDNA, wherein SEQ ID NO:1679 is a clone designated herein as "DNA328034".

30       Figure 1680 shows the amino acid sequence (SEQ ID NO:1680) derived from the coding sequence of SEQ ID NO:1679 shown in Figure 1679.

Figure 1681 shows a nucleotide sequence (SEQ ID NO:1681) of a native sequence PRO83951 cDNA, wherein SEQ ID NO:1681 is a clone designated herein as "DNA328035".

Figure 1682 shows the amino acid sequence (SEQ ID NO:1682) derived from the coding sequence of SEQ ID NO:1681 shown in Figure 1681.

35       Figure 1683 shows a nucleotide sequence (SEQ ID NO:1683) of a native sequence cDNA, wherein SEQ ID NO:1683 is a clone designated herein as "DNA328036".

Figure 1684 shows a nucleotide sequence (SEQ ID NO:1684) of a native sequence cDNA, wherein SEQ ID NO:1684 is a clone designated herein as "DNA328037".

40       Figure 1685 shows a nucleotide sequence (SEQ ID NO:1685) of a native sequence PRO83953 cDNA, wherein SEQ ID NO:1685 is a clone designated herein as "DNA328038".

Figure 1686 shows the amino acid sequence (SEQ ID NO:1686) derived from the coding sequence of SEQ ID NO:1685 shown in Figure 1685.

Figure 1687 shows a nucleotide sequence (SEQ ID NO:1687) of a native sequence PRO83954 cDNA, wherein SEQ ID NO:1687 is a clone designated herein as "DNA328039".

5 Figure 1688 shows the amino acid sequence (SEQ ID NO:1688) derived from the coding sequence of SEQ ID NO:1687 shown in Figure 1677.

Figure 1689 shows a nucleotide sequence (SEQ ID NO:1689) of a native sequence cDNA, wherein SEQ ID NO:1689 is a clone designated herein as "DNA328040".

10 Figure 1690 shows a nucleotide sequence (SEQ ID NO:1690) of a native sequence PRO83955 cDNA, wherein SEQ ID NO:1690 is a clone designated herein as "DNA328041".

Figure 1691 shows the amino acid sequence (SEQ ID NO:1691) derived from the coding sequence of SEQ ID NO:1690 shown in Figure 1690.

Figure 1692 shows a nucleotide sequence (SEQ ID NO:1692) of a native sequence PRO83956 cDNA, wherein SEQ ID NO:1692 is a clone designated herein as "DNA328042".

15 Figure 1693 shows the amino acid sequence (SEQ ID NO:1693) derived from the coding sequence of SEQ ID NO:1692 shown in Figure 1692.

Figure 1694 shows a nucleotide sequence (SEQ ID NO:1694) of a native sequence PRO83957 cDNA, wherein SEQ ID NO:1694 is a clone designated herein as "DNA328043".

20 Figure 1695 shows the amino acid sequence (SEQ ID NO:1695) derived from the coding sequence of SEQ ID NO:1694 shown in Figure 1694.

Figure 1696 shows a nucleotide sequence (SEQ ID NO:1696) of a native sequence PRO83958 cDNA, wherein SEQ ID NO:1696 is a clone designated herein as "DNA328044".

Figure 1697 shows the amino acid sequence (SEQ ID NO:1697) derived from the coding sequence of SEQ ID NO:1696 shown in Figure 1696.

25 Figure 1698 shows a nucleotide sequence (SEQ ID NO:1698) of a native sequence PRO83959 cDNA, wherein SEQ ID NO:1698 is a clone designated herein as "DNA328045".

Figure 1699 shows the amino acid sequence (SEQ ID NO:1699) derived from the coding sequence of SEQ ID NO:1698 shown in Figure 1698.

30 Figure 1700 shows a nucleotide sequence (SEQ ID NO:1700) of a native sequence PRO83960 cDNA, wherein SEQ ID NO:1700 is a clone designated herein as "DNA328046".

Figure 1701 shows the amino acid sequence (SEQ ID NO:1701) derived from the coding sequence of SEQ ID NO:1700 shown in Figure 1700.

Figure 1702 shows a nucleotide sequence (SEQ ID NO:1702) of a native sequence PRO83961 cDNA, wherein SEQ ID NO:1702 is a clone designated herein as "DNA328047".

35 Figure 1703 shows the amino acid sequence (SEQ ID NO:1703) derived from the coding sequence of SEQ ID NO:1702 shown in Figure 1702.

Figure 1704 shows a nucleotide sequence (SEQ ID NO:1704) of a native sequence PRO83962 cDNA, wherein SEQ ID NO:1704 is a clone designated herein as "DNA328048".

40 Figure 1705 shows the amino acid sequence (SEQ ID NO:1705) derived from the coding sequence of SEQ ID NO:1704 shown in Figure 1704.

Figure 1706 shows a nucleotide sequence (SEQ ID NO:1706) of a native sequence cDNA, wherein SEQ ID NO:1706 is a clone designated herein as "DNA257403".

Figure 1707 shows a nucleotide sequence (SEQ ID NO:1707) of a native sequence PRO23317 cDNA, wherein SEQ ID NO:1707 is a clone designated herein as "DNA193899".

5        Figure 1708 shows the amino acid sequence (SEQ ID NO:1708) derived from the coding sequence of SEQ ID NO:1707 shown in Figure 1707.

Figure 1709 shows a nucleotide sequence (SEQ ID NO:1709) of a native sequence PRO83963 cDNA, wherein SEQ ID NO:1709 is a clone designated herein as "DNA328049".

10       Figure 1710 shows the amino acid sequence (SEQ ID NO:1710) derived from the coding sequence of SEQ ID NO:1709 shown in Figure 1709.

Figure 1711 shows a nucleotide sequence (SEQ ID NO:1711) of a native sequence PRO60890 cDNA, wherein SEQ ID NO:1711 is a clone designated herein as "DNA272784".

Figure 1712 shows the amino acid sequence (SEQ ID NO:1712) derived from the coding sequence of SEQ ID NO:1711 shown in Figure 1711.

15       Figure 1713 shows a nucleotide sequence (SEQ ID NO:1713) of a native sequence PRO49544 cDNA, wherein SEQ ID NO:1713 is a clone designated herein as "DNA254435".

Figure 1714 shows the amino acid sequence (SEQ ID NO:1714) derived from the coding sequence of SEQ ID NO:1713 shown in Figure 1713.

20       Figure 1715 shows a nucleotide sequence (SEQ ID NO:1715) of a native sequence PRO83964 cDNA, wherein SEQ ID NO:1715 is a clone designated herein as "DNA328050".

Figure 1716 shows the amino acid sequence (SEQ ID NO:1716) derived from the coding sequence of SEQ ID NO:1715 shown in Figure 1715.

Figure 1717 shows a nucleotide sequence (SEQ ID NO:1717) of a native sequence PRO83965 cDNA, wherein SEQ ID NO:1717 is a clone designated herein as "DNA328051".

25       Figure 1718 shows the amino acid sequence (SEQ ID NO:1718) derived from the coding sequence of SEQ ID NO:1717 shown in Figure 1717.

Figure 1719 shows a nucleotide sequence (SEQ ID NO:1719) of a native sequence PRO83966 cDNA, wherein SEQ ID NO:1719 is a clone designated herein as "DNA328052".

30       Figure 1720 shows the amino acid sequence (SEQ ID NO:1720) derived from the coding sequence of SEQ ID NO:1719 shown in Figure 1719.

Figure 1721 shows a nucleotide sequence (SEQ ID NO:1721) of a native sequence PRO61074 cDNA, wherein SEQ ID NO:1721 is a clone designated herein as "DNA273002".

Figure 1722 shows the amino acid sequence (SEQ ID NO:1722) derived from the coding sequence of SEQ ID NO:1721 shown in Figure 1721.

35       Figure 1723 shows a nucleotide sequence (SEQ ID NO:1723) of a native sequence cDNA, wherein SEQ ID NO:1723 is a clone designated herein as "DNA164635".

Figure 1724 shows a nucleotide sequence (SEQ ID NO:1724) of a native sequence PRO83967 cDNA, wherein SEQ ID NO:1724 is a clone designated herein as "DNA328053".

40       Figure 1725 shows the amino acid sequence (SEQ ID NO:1725) derived from the coding sequence of SEQ ID NO:1724 shown in Figure 1724.

Figure 1726 shows a nucleotide sequence (SEQ ID NO:1726) of a native sequence PRO19908 cDNA, wherein SEQ ID NO:1726 is a clone designated herein as "DNA76526".

Figure 1727 shows the amino acid sequence (SEQ ID NO:1727) derived from the coding sequence of SEQ ID NO:1726 shown in Figure 1726.

5 Figure 1728 shows a nucleotide sequence (SEQ ID NO:1728) of a native sequence PRO11861 cDNA, wherein SEQ ID NO:1728 is a clone designated herein as "DNA151516".

Figure 1729 shows the amino acid sequence (SEQ ID NO:1729) derived from the coding sequence of SEQ ID NO:1728 shown in Figure 1728.

10 Figure 1730 shows a nucleotide sequence (SEQ ID NO:1730) of a native sequence PRO83968 cDNA, wherein SEQ ID NO:1730 is a clone designated herein as "DNA328054".

Figure 1731 shows the amino acid sequence (SEQ ID NO:1731) derived from the coding sequence of SEQ ID NO:1730 shown in Figure 1730.

Figure 1732 shows a nucleotide sequence (SEQ ID NO:1732) of a native sequence PRO83969 cDNA, wherein SEQ ID NO:1732 is a clone designated herein as "DNA328055".

15 Figure 1733 shows the amino acid sequence (SEQ ID NO:1733) derived from the coding sequence of SEQ ID NO:1732 shown in Figure 1732.

Figure 1734 shows a nucleotide sequence (SEQ ID NO:1734) of a native sequence PRO83970 cDNA, wherein SEQ ID NO:1734 is a clone designated herein as "DNA328056".

20 Figure 1735 shows the amino acid sequence (SEQ ID NO:1735) derived from the coding sequence of SEQ ID NO:1734 shown in Figure 1734.

Figure 1736 shows a nucleotide sequence (SEQ ID NO:1736) of a native sequence cDNA, wherein ~~SEQ ID NO:1736 is a clone designated herein as "DNA328057".~~

Figure 1737 shows a nucleotide sequence (SEQ ID NO:1737) of a native sequence PRO83971 cDNA, wherein SEQ ID NO:1737 is a clone designated herein as "DNA328058".

25 Figure 1738 shows the amino acid sequence (SEQ ID NO:1738) derived from the coding sequence of SEQ ID NO:1737 shown in Figure 1737.

Figure 1739 shows a nucleotide sequence (SEQ ID NO:1739) of a native sequence PRO52268 cDNA, wherein SEQ ID NO:1739 is a clone designated herein as "DNA257714".

30 Figure 1740 shows the amino acid sequence (SEQ ID NO:1740) derived from the coding sequence of SEQ ID NO:1739 shown in Figure 1739.

Figure 1741 shows a nucleotide sequence (SEQ ID NO:1741) of a native sequence PRO83972 cDNA, wherein SEQ ID NO:1741 is a clone designated herein as "DNA328059".

Figure 1742 shows the amino acid sequence (SEQ ID NO:1742) derived from the coding sequence of SEQ ID NO:1741 shown in Figure 1741.

35 Figure 1743 shows a nucleotide sequence (SEQ ID NO:1743) of a native sequence PRO83973 cDNA, wherein SEQ ID NO:1743 is a clone designated herein as "DNA328060".

Figure 1744 shows the amino acid sequence (SEQ ID NO:1744) derived from the coding sequence of SEQ ID NO:1743 shown in Figure 1743.

40 Figure 1745 shows a nucleotide sequence (SEQ ID NO:1745) of a native sequence PRO83974 cDNA, wherein SEQ ID NO:1745 is a clone designated herein as "DNA328061".

Figure 1746 shows the amino acid sequence (SEQ ID NO:1746) derived from the coding sequence of SEQ ID NO:1745 shown in Figure 1745.

Figure 1747 shows a nucleotide sequence (SEQ ID NO:1747) of a native sequence PRO83975 cDNA, wherein SEQ ID NO:1747 is a clone designated herein as "DNA328062".

5        Figure 1748 shows the amino acid sequence (SEQ ID NO:1748) derived from the coding sequence of SEQ ID NO:1747 shown in Figure 1747.

Figure 1749 shows a nucleotide sequence (SEQ ID NO:1749) of a native sequence PRO83976 cDNA, wherein SEQ ID NO:1749 is a clone designated herein as "DNA328063".

10       Figure 1750 shows the amino acid sequence (SEQ ID NO:1750) derived from the coding sequence of SEQ ID NO:1749 shown in Figure 1749.

Figure 1751 shows a nucleotide sequence (SEQ ID NO:1751) of a native sequence PRO3446 cDNA, wherein SEQ ID NO:1751 is a clone designated herein as "DNA92219".

Figure 1752 shows the amino acid sequence (SEQ ID NO:1752) derived from the coding sequence of SEQ ID NO:1751 shown in Figure 1751.

15       Figure 1753 shows a nucleotide sequence (SEQ ID NO:1753) of a native sequence PRO83977 cDNA, wherein SEQ ID NO:1753 is a clone designated herein as "DNA328064".

Figure 1754 shows the amino acid sequence (SEQ ID NO:1754) derived from the coding sequence of SEQ ID NO:1753 shown in Figure 1753.

20       Figure 1755 shows a nucleotide sequence (SEQ ID NO:1755) of a native sequence PRO83978 cDNA, wherein SEQ ID NO:1755 is a clone designated herein as "DNA328065".

Figure 1756 shows the amino acid sequence (SEQ ID NO:1756) derived from the coding sequence of SEQ ID NO:1755 shown in Figure 1755.

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Figure 1757 shows a nucleotide sequence (SEQ ID NO:1757) of a native sequence PRO1107 cDNA, wherein SEQ ID NO:1757 is a clone designated herein as "DNA59606".

25       Figure 1758 shows the amino acid sequence (SEQ ID NO:1758) derived from the coding sequence of SEQ ID NO:1757 shown in Figure 1757.

Figure 1759 shows a nucleotide sequence (SEQ ID NO:1759) of a native sequence PRO83979 cDNA, wherein SEQ ID NO:1759 is a clone designated herein as "DNA328066".

30       Figure 1760 shows the amino acid sequence (SEQ ID NO:1760) derived from the coding sequence of SEQ ID NO:1759 shown in Figure 1759.

Figure 1761 shows a nucleotide sequence (SEQ ID NO:1761) of a native sequence PRO83980 cDNA, wherein SEQ ID NO:1761 is a clone designated herein as "DNA328067".

Figure 1762 shows the amino acid sequence (SEQ ID NO:1762) derived from the coding sequence of SEQ ID NO:1761 shown in Figure 1761.

35       Figure 1763 shows a nucleotide sequence (SEQ ID NO:1763) of a native sequence PRO83981 cDNA, wherein SEQ ID NO:1763 is a clone designated herein as "DNA328068".

Figure 1764 shows the amino acid sequence (SEQ ID NO:1764) derived from the coding sequence of SEQ ID NO:1763 shown in Figure 1763.

40       Figure 1765 shows a nucleotide sequence (SEQ ID NO:1765) of a native sequence cDNA, wherein SEQ ID NO:1765 is a clone designated herein as "DNA161182".

Figure 1766 shows a nucleotide sequence (SEQ ID NO:1766) of a native sequence PRO363 cDNA, wherein SEQ ID NO:1766 is a clone designated herein as "DNA328069".

Figure 1767 shows the amino acid sequence (SEQ ID NO:1767) derived from the coding sequence of SEQ ID NO:1766 shown in Figure 1766.

5        Figure 1768 shows a nucleotide sequence (SEQ ID NO:1768) of a native sequence PRO83982 cDNA, wherein SEQ ID NO:1768 is a clone designated herein as "DNA328070".

Figure 1769 shows the amino acid sequence (SEQ ID NO:1769) derived from the coding sequence of SEQ ID NO:1768 shown in Figure 1768.

10       Figure 1770 shows a nucleotide sequence (SEQ ID NO:1770) of a native sequence PRO83983 cDNA, wherein SEQ ID NO:1770 is a clone designated herein as "DNA328071".

Figure 1771 shows the amino acid sequence (SEQ ID NO:1771) derived from the coding sequence of SEQ ID NO:1770 shown in Figure 1770.

Figure 1772 shows a nucleotide sequence (SEQ ID NO:1772) of a native sequence cDNA, wherein SEQ ID NO:1772 is a clone designated herein as "DNA328072".

15       Figure 1773 shows a nucleotide sequence (SEQ ID NO:1773) of a native sequence PRO83985 cDNA, wherein SEQ ID NO:1773 is a clone designated herein as "DNA328073".

Figure 1774 shows the amino acid sequence (SEQ ID NO:1774) derived from the coding sequence of SEQ ID NO:1773 shown in Figure 1773.

20       Figure 1775 shows a nucleotide sequence (SEQ ID NO:1775) of a native sequence PRO54700 cDNA, wherein SEQ ID NO:1775 is a clone designated herein as "DNA260948".

Figure 1776 shows the amino acid sequence (SEQ ID NO:1776) derived from the coding sequence of SEQ ID NO:1775 shown in Figure 1775.

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Figure 1777 shows a nucleotide sequence (SEQ ID NO:1777) of a native sequence cDNA, wherein SEQ ID NO:1777 is a clone designated herein as "DNA328074".

25       Figure 1778 shows a nucleotide sequence (SEQ ID NO:1778) of a native sequence PRO23594 cDNA, wherein SEQ ID NO:1778 is a clone designated herein as "DNA194202".

Figure 1779 shows the amino acid sequence (SEQ ID NO:1779) derived from the coding sequence of SEQ ID NO:1778 shown in Figure 1778.

30       Figure 1780 shows a nucleotide sequence (SEQ ID NO:1780) of a native sequence cDNA, wherein SEQ ID NO:1780 is a clone designated herein as "DNA328075".

Figure 1781 shows a nucleotide sequence (SEQ ID NO:1781) of a native sequence PRO83988 cDNA, wherein SEQ ID NO:1781 is a clone designated herein as "DNA328076".

Figure 1782 shows the amino acid sequence (SEQ ID NO:1782) derived from the coding sequence of SEQ ID NO:1781 shown in Figure 1781.

35       Figure 1783 shows a nucleotide sequence (SEQ ID NO:1783) of a native sequence PRO83989 cDNA, wherein SEQ ID NO:1783 is a clone designated herein as "DNA328077".

Figure 1784 shows the amino acid sequence (SEQ ID NO:1784) derived from the coding sequence of SEQ ID NO:1783 shown in Figure 1783.

40       Figure 1785 shows a nucleotide sequence (SEQ ID NO:1785) of a native sequence PRO11946 cDNA, wherein SEQ ID NO:1785 is a clone designated herein as "DNA151638".

Figure 1786 shows the amino acid sequence (SEQ ID NO:1786) derived from the coding sequence of SEQ ID NO:1785 shown in Figure 1785.

Figure 1787 shows a nucleotide sequence (SEQ ID NO:1787) of a native sequence cDNA, wherein SEQ ID NO:1787 is a clone designated herein as "DNA195938".

5        Figure 1788 shows a nucleotide sequence (SEQ ID NO:1788) of a native sequence PRO83990 cDNA, wherein SEQ ID NO:1788 is a clone designated herein as "DNA328078".

Figure 1789 shows the amino acid sequence (SEQ ID NO:1789) derived from the coding sequence of SEQ ID NO:1788 shown in Figure 1788.

10       Figure 1790 shows a nucleotide sequence (SEQ ID NO:1790) of a native sequence PRO83991 cDNA, wherein SEQ ID NO:1790 is a clone designated herein as "DNA328079".

Figure 1791 shows the amino acid sequence (SEQ ID NO:1791) derived from the coding sequence of SEQ ID NO:1790 shown in Figure 1790.

Figure 1792 shows a nucleotide sequence (SEQ ID NO:1792) of a native sequence cDNA, wherein SEQ ID NO:1792 is a clone designated herein as "DNA257517".

15       Figure 1793 shows a nucleotide sequence (SEQ ID NO:1793) of a native sequence PRO83992 cDNA, wherein SEQ ID NO:1793 is a clone designated herein as "DNA328080".

Figure 1794 shows the amino acid sequence (SEQ ID NO:1794) derived from the coding sequence of SEQ ID NO:1793 shown in Figure 1793.

20       Figure 1795 shows a nucleotide sequence (SEQ ID NO:1795) of a native sequence PRO83993 cDNA, wherein SEQ ID NO:1795 is a clone designated herein as "DNA328081".

Figure 1796 shows the amino acid sequence (SEQ ID NO:1796) derived from the coding sequence of SEQ ID NO:1795 shown in Figure 1795.

Figure 1797 shows a nucleotide sequence (SEQ ID NO:1797) of a native sequence PRO83994 cDNA, wherein SEQ ID NO:1797 is a clone designated herein as "DNA328082".

25       Figure 1798 shows the amino acid sequence (SEQ ID NO:1798) derived from the coding sequence of SEQ ID NO:1797 shown in Figure 1797.

Figure 1799 shows a nucleotide sequence (SEQ ID NO:1799) of a native sequence PRO83995 cDNA, wherein SEQ ID NO:1799 is a clone designated herein as "DNA328083".

30       Figure 1800 shows the amino acid sequence (SEQ ID NO:1800) derived from the coding sequence of SEQ ID NO:1799 shown in Figure 1799.

Figure 1801 shows a nucleotide sequence (SEQ ID NO:1801) of a native sequence PRO37611 cDNA, wherein SEQ ID NO:1801 is a clone designated herein as "DNA227148".

Figure 1802 shows the amino acid sequence (SEQ ID NO:1802) derived from the coding sequence of SEQ ID NO:1801 shown in Figure 1801.

35       Figure 1803 shows a nucleotide sequence (SEQ ID NO:1803) of a native sequence PRO83996 cDNA, wherein SEQ ID NO:1803 is a clone designated herein as "DNA328084".

Figure 1804 shows the amino acid sequence (SEQ ID NO:1804) derived from the coding sequence of SEQ ID NO:1803 shown in Figure 1803.

40       Figure 1805 shows a nucleotide sequence (SEQ ID NO:1805) of a native sequence PRO83997 cDNA, wherein SEQ ID NO:1805 is a clone designated herein as "DNA328085".



Figure 1806 shows the amino acid sequence (SEQ ID NO:1806) derived from the coding sequence of SEQ ID NO:1805 shown in Figure 1805.

Figure 1807 shows a nucleotide sequence (SEQ ID NO:1807) of a native sequence PRO34934 cDNA, wherein SEQ ID NO:1807 is a clone designated herein as "DNA328086".

5 Figure 1808 shows the amino acid sequence (SEQ ID NO:1808) derived from the coding sequence of SEQ ID NO:1807 shown in Figure 1807.

Figure 1809 shows a nucleotide sequence (SEQ ID NO:1809) of a native sequence PRO83998 cDNA, wherein SEQ ID NO:1809 is a clone designated herein as "DNA328087".

10 Figure 1810 shows the amino acid sequence (SEQ ID NO:1810) derived from the coding sequence of SEQ ID NO:1809 shown in Figure 1809.

Figure 1811 shows a nucleotide sequence (SEQ ID NO:1811) of a native sequence PRO83999 cDNA, wherein SEQ ID NO:1811 is a clone designated herein as "DNA328088".

Figure 1812 shows the amino acid sequence (SEQ ID NO:1812) derived from the coding sequence of SEQ ID NO:1811 shown in Figure 1811.

15 Figure 1813 shows a nucleotide sequence (SEQ ID NO:1813) of a native sequence PRO84000 cDNA, wherein SEQ ID NO:1813 is a clone designated herein as "DNA328089".

Figure 1814 shows the amino acid sequence (SEQ ID NO:1814) derived from the coding sequence of SEQ ID NO:1813 shown in Figure 1813.

20 Figure 1815 shows a nucleotide sequence (SEQ ID NO:1815) of a native sequence PRO84001 cDNA, wherein SEQ ID NO:1815 is a clone designated herein as "DNA328090".

Figure 1816 shows the amino acid sequence (SEQ ID NO:1816) derived from the coding sequence of SEQ ID NO:1815 shown in Figure 1815.

Figure 1817 shows a nucleotide sequence (SEQ ID NO:1817) of a native sequence PRO84002 cDNA, wherein SEQ ID NO:1817 is a clone designated herein as "DNA328091".

25 Figure 1818 shows the amino acid sequence (SEQ ID NO:1818) derived from the coding sequence of SEQ ID NO:1817 shown in Figure 1817.

Figure 1819 shows a nucleotide sequence (SEQ ID NO:1819) of a native sequence PRO84003 cDNA, wherein SEQ ID NO:1819 is a clone designated herein as "DNA328092".

30 Figure 1820 shows the amino acid sequence (SEQ ID NO:1820) derived from the coding sequence of SEQ ID NO:1819 shown in Figure 1819.

Figure 1821 shows a nucleotide sequence (SEQ ID NO:1821) of a native sequence PRO37631 cDNA, wherein SEQ ID NO:1821 is a clone designated herein as "DNA227168".

Figure 1822 shows the amino acid sequence (SEQ ID NO:1822) derived from the coding sequence of SEQ ID NO:1821 shown in Figure 1821.

35 Figure 1823 shows a nucleotide sequence (SEQ ID NO:1823) of a native sequence PRO84004 cDNA, wherein SEQ ID NO:1823 is a clone designated herein as "DNA328093".

Figure 1824 shows the amino acid sequence (SEQ ID NO:1824) derived from the coding sequence of SEQ ID NO:1823 shown in Figure 1823.

40 Figure 1825 shows a nucleotide sequence (SEQ ID NO:1825) of a native sequence PRO84005 cDNA, wherein SEQ ID NO:1825 is a clone designated herein as "DNA328094".

Figure 1826 shows the amino acid sequence (SEQ ID NO:1826) derived from the coding sequence of SEQ ID NO:1825 shown in Figure 1825.

Figure 1827 shows a nucleotide sequence (SEQ ID NO:1827) of a native sequence PRO50404 cDNA, wherein SEQ ID NO:1827 is a clone designated herein as "DNA255334".

5        Figure 1828 shows the amino acid sequence (SEQ ID NO:1828) derived from the coding sequence of SEQ ID NO:1827 shown in Figure 1827.

Figure 1829 shows a nucleotide sequence (SEQ ID NO:1829) of a native sequence PRO84006 cDNA, wherein SEQ ID NO:1829 is a clone designated herein as "DNA328095".

10       Figure 1830 shows the amino acid sequence (SEQ ID NO:1830) derived from the coding sequence of SEQ ID NO:1829 shown in Figure 1829.

Figure 1831 shows a nucleotide sequence (SEQ ID NO:1831) of a native sequence PRO84007 cDNA, wherein SEQ ID NO:1831 is a clone designated herein as "DNA328096".

Figure 1832 shows the amino acid sequence (SEQ ID NO:1832) derived from the coding sequence of SEQ ID NO:1831 shown in Figure 1831.

15       Figure 1833 shows a nucleotide sequence (SEQ ID NO:1833) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:1833 is a clone designated herein as "DNA328097".

Figure 1834 shows the amino acid sequence (SEQ ID NO:1834) derived from the coding sequence of SEQ ID NO: shown in Figure 1833.

20       Figure 1835 shows a nucleotide sequence (SEQ ID NO:1835) of a native sequence PRO84008 cDNA, wherein SEQ ID NO:1835 is a clone designated herein as "DNA328098".

Figure 1836 shows the amino acid sequence (SEQ ID NO:1836) derived from the coding sequence of SEQ ID NO:1835 shown in Figure 1835.

Figure 1837 shows a nucleotide sequence (SEQ ID NO:1837) of a native sequence PRO84009 cDNA, wherein SEQ ID NO:1837 is a clone designated herein as "DNA328099".

25       Figure 1838 shows the amino acid sequence (SEQ ID NO:1838) derived from the coding sequence of SEQ ID NO:1837 shown in Figure 1837.

Figure 1839 shows a nucleotide sequence (SEQ ID NO:1839) of a native sequence PRO84010 cDNA, wherein SEQ ID NO:1839 is a clone designated herein as "DNA328100".

30       Figure 1840 shows the amino acid sequence (SEQ ID NO:1840) derived from the coding sequence of SEQ ID NO:1839 shown in Figure 1839.

Figure 1841 shows a nucleotide sequence (SEQ ID NO:1841) of a native sequence PRO84011 cDNA, wherein SEQ ID NO:1841 is a clone designated herein as "DNA328101".

Figure 1842 shows the amino acid sequence (SEQ ID NO:1842) derived from the coding sequence of SEQ ID NO:1841 shown in Figure 1841.

35       Figure 1843 shows a nucleotide sequence (SEQ ID NO:1843) of a native sequence PRO84012 cDNA, wherein SEQ ID NO:1843 is a clone designated herein as "DNA328102".

Figure 1844 shows the amino acid sequence (SEQ ID NO:1844) derived from the coding sequence of SEQ ID NO:1843 shown in Figure 1843.

40       Figure 1845 shows a nucleotide sequence (SEQ ID NO:1845) of a native sequence PRO84013 cDNA, wherein SEQ ID NO:1845 is a clone designated herein as "DNA328103".

Figure 1846 shows the amino acid sequence (SEQ ID NO:1846) derived from the coding sequence of SEQ ID NO:1845 shown in Figure 1845.

Figure 1847 shows a nucleotide sequence (SEQ ID NO:1847) of a native sequence PRO84014 cDNA, wherein SEQ ID NO:1847 is a clone designated herein as "DNA328104".

5 Figure 1848 shows the amino acid sequence (SEQ ID NO:1848) derived from the coding sequence of SEQ ID NO:1847 shown in Figure 1847.

Figure 1849 shows a nucleotide sequence (SEQ ID NO:1849) of a native sequence PRO84015 cDNA, wherein SEQ ID NO:1849 is a clone designated herein as "DNA328105".

10 Figure 1850 shows the amino acid sequence (SEQ ID NO:1850) derived from the coding sequence of SEQ ID NO:1849 shown in Figure 1849.

Figure 1851 shows a nucleotide sequence (SEQ ID NO:1851) of a native sequence PRO19611 cDNA, wherein SEQ ID NO:1851 is a clone designated herein as "DNA328106".

Figure 1852 shows the amino acid sequence (SEQ ID NO:1852) derived from the coding sequence of SEQ ID NO:1851 shown in Figure 1851.

15 Figure 1853 shows a nucleotide sequence (SEQ ID NO:1853) of a native sequence cDNA, wherein SEQ ID NO:1853 is a clone designated herein as "DNA195707".

Figure 1854 shows a nucleotide sequence (SEQ ID NO:1854) of a native sequence cDNA, wherein SEQ ID NO:1854 is a clone designated herein as "DNA328107".

20 Figure 1855 shows a nucleotide sequence (SEQ ID NO:1855) of a native sequence PRO84016 cDNA, wherein SEQ ID NO:1855 is a clone designated herein as "DNA328108".

Figure 1856 shows the amino acid sequence (SEQ ID NO:1856) derived from the coding sequence of SEQ ID NO:1855 shown in Figure 1855.

Figure 1857 shows a nucleotide sequence (SEQ ID NO:1857) of a native sequence PRO84017 cDNA, wherein SEQ ID NO:1857 is a clone designated herein as "DNA328109".

25 Figure 1858 shows the amino acid sequence (SEQ ID NO:1858) derived from the coding sequence of SEQ ID NO:1857 shown in Figure 1857.

Figure 1859 shows a nucleotide sequence (SEQ ID NO:1859) of a native sequence PRO84018 cDNA, wherein SEQ ID NO:1859 is a clone designated herein as "DNA328110".

30 Figure 1860 shows the amino acid sequence (SEQ ID NO:1860) derived from the coding sequence of SEQ ID NO:1859 shown in Figure 1859.

Figure 1861 shows a nucleotide sequence (SEQ ID NO:1861) of a native sequence PRO4327 cDNA, wherein SEQ ID NO:1861 is a clone designated herein as "DNA328111".

Figure 1862 shows the amino acid sequence (SEQ ID NO:1862) derived from the coding sequence of SEQ ID NO:1861 shown in Figure 1861.

35 Figure 1863 shows a nucleotide sequence (SEQ ID NO:1863) of a native sequence PRO60060 cDNA, wherein SEQ ID NO:1863 is a clone designated herein as "DNA271776".

Figure 1864 shows the amino acid sequence (SEQ ID NO:1864) derived from the coding sequence of SEQ ID NO:1863 shown in Figure 1863.

40 Figure 1865 shows a nucleotide sequence (SEQ ID NO:1865) of a native sequence cDNA, wherein SEQ ID NO:1865 is a clone designated herein as "DNA328112".

Figure 1866 shows a nucleotide sequence (SEQ ID NO:1866) of a native sequence PRO84020 cDNA, wherein SEQ ID NO:1866 is a clone designated herein as "DNA328113".

Figure 1867 shows the amino acid sequence (SEQ ID NO:1867) derived from the coding sequence of SEQ ID NO:1866 shown in Figure 1866.

5        Figure 1868 shows a nucleotide sequence (SEQ ID NO:1868) of a native sequence PRO84021 cDNA, wherein SEQ ID NO:1868 is a clone designated herein as "DNA328114".

Figure 1869 shows the amino acid sequence (SEQ ID NO:1869) derived from the coding sequence of SEQ ID NO:1868 shown in Figure 1868.

10        Figure 1870 shows a nucleotide sequence (SEQ ID NO:1870) of a native sequence PRO84022 cDNA, wherein SEQ ID NO:1870 is a clone designated herein as "DNA328115".

Figure 1871 shows the amino acid sequence (SEQ ID NO:1871) derived from the coding sequence of SEQ ID NO:1870 shown in Figure 1870.

Figure 1872 shows a nucleotide sequence (SEQ ID NO:1872) of a native sequence PRO84023 cDNA, wherein SEQ ID NO:1872 is a clone designated herein as "DNA328116".

15        Figure 1873 shows the amino acid sequence (SEQ ID NO:1873) derived from the coding sequence of SEQ ID NO:1872 shown in Figure 1872.

Figure 1874 shows a nucleotide sequence (SEQ ID NO:1874) of a native sequence cDNA, wherein SEQ ID NO:1874 is a clone designated herein as "DNA256068".

20        Figure 1875 shows a nucleotide sequence (SEQ ID NO:1875) of a native sequence PRO84024 cDNA, wherein SEQ ID NO:1875 is a clone designated herein as "DNA328117".

Figure 1876 shows the amino acid sequence (SEQ ID NO:1876) derived from the coding sequence of SEQ ID NO:1875 shown in Figure 1875.

Figure 1877 shows a nucleotide sequence (SEQ ID NO:1877) of a native sequence PRO84025 cDNA, wherein SEQ ID NO:1877 is a clone designated herein as "DNA328118".

25        Figure 1878 shows the amino acid sequence (SEQ ID NO:1878) derived from the coding sequence of SEQ ID NO:1877 shown in Figure 1877.

Figure 1879 shows a nucleotide sequence (SEQ ID NO:1879) of a native sequence PRO84026 cDNA, wherein SEQ ID NO:1879 is a clone designated herein as "DNA328119".

30        Figure 1880 shows the amino acid sequence (SEQ ID NO:1880) derived from the coding sequence of SEQ ID NO:1879 shown in Figure 1879.

Figure 1881 shows a nucleotide sequence (SEQ ID NO:1881) of a native sequence cDNA, wherein SEQ ID NO:1881 is a clone designated herein as "DNA328120".

Figure 1882 shows a nucleotide sequence (SEQ ID NO:1882) of a native sequence PRO84028 cDNA, wherein SEQ ID NO:1882 is a clone designated herein as "DNA328121".

35        Figure 1883 shows the amino acid sequence (SEQ ID NO:1883) derived from the coding sequence of SEQ ID NO:1882 shown in Figure 1882.

Figure 1884 shows a nucleotide sequence (SEQ ID NO:1884) of a native sequence PRO84029 cDNA, wherein SEQ ID NO:1884 is a clone designated herein as "DNA328122".

40        Figure 1885 shows the amino acid sequence (SEQ ID NO:1885) derived from the coding sequence of SEQ ID NO:1884 shown in Figure 1884.

Figure 1886 shows a nucleotide sequence (SEQ ID NO:1886) of a native sequence PRO84030 cDNA, wherein SEQ ID NO:1886 is a clone designated herein as "DNA328123".

Figure 1887 shows the amino acid sequence (SEQ ID NO:1887) derived from the coding sequence of SEQ ID NO:1886 shown in Figure 1886.

5        Figure 1888 shows a nucleotide sequence (SEQ ID NO:1888) of a native sequence cDNA, wherein SEQ ID NO:1888 is a clone designated herein as "DNA328124".

Figure 1889 shows a nucleotide sequence (SEQ ID NO:1889) of a native sequence PRO84031 cDNA, wherein SEQ ID NO:1889 is a clone designated herein as "DNA328125".

10       Figure 1890 shows the amino acid sequence (SEQ ID NO:1890) derived from the coding sequence of SEQ ID NO:1889 shown in Figure 1889.

Figure 1891 shows a nucleotide sequence (SEQ ID NO:1891) of a native sequence PRO84032 cDNA, wherein SEQ ID NO:1891 is a clone designated herein as "DNA328126".

Figure 1892 shows the amino acid sequence (SEQ ID NO:1892) derived from the coding sequence of SEQ ID NO:1891 shown in Figure 1891.

15       Figure 1893 shows a nucleotide sequence (SEQ ID NO:1893) of a native sequence PRO84033 cDNA, wherein SEQ ID NO:1893 is a clone designated herein as "DNA328127".

Figure 1894 shows the amino acid sequence (SEQ ID NO:1894) derived from the coding sequence of SEQ ID NO:1893 shown in Figure 1893.

20       Figure 1895 shows a nucleotide sequence (SEQ ID NO:1895) of a native sequence PRO84034 cDNA, wherein SEQ ID NO:1895 is a clone designated herein as "DNA328128".

Figure 1896 shows the amino acid sequence (SEQ ID NO:1896) derived from the coding sequence of SEQ ID NO:1895 shown in Figure 1895.

Figure 1897 shows a nucleotide sequence (SEQ ID NO:1897) of a native sequence PRO84035 cDNA, wherein SEQ ID NO:1897 is a clone designated herein as "DNA328129".

25       Figure 1898 shows the amino acid sequence (SEQ ID NO:1898) derived from the coding sequence of SEQ ID NO:1897 shown in Figure 1897.

Figure 1899 shows a nucleotide sequence (SEQ ID NO:1899) of a native sequence PRO84036 cDNA, wherein SEQ ID NO:1899 is a clone designated herein as "DNA328130".

30       Figure 1900 shows the amino acid sequence (SEQ ID NO:1900) derived from the coding sequence of SEQ ID NO:1899 shown in Figure 1899.

Figure 1901 shows a nucleotide sequence (SEQ ID NO:1901) of a native sequence PRO84037 cDNA, wherein SEQ ID NO:1901 is a clone designated herein as "DNA328131".

Figure 1902 shows the amino acid sequence (SEQ ID NO:1902) derived from the coding sequence of SEQ ID NO:1901 shown in Figure 1901.

35       Figure 1903 shows a nucleotide sequence (SEQ ID NO:1903) of a native sequence PRO84038 cDNA, wherein SEQ ID NO:1903 is a clone designated herein as "DNA328132".

Figure 1904 shows the amino acid sequence (SEQ ID NO:1904) derived from the coding sequence of SEQ ID NO:1903 shown in Figure 1903.

40       Figure 1905 shows a nucleotide sequence (SEQ ID NO:1905) of a native sequence PRO84039 cDNA, wherein SEQ ID NO:1905 is a clone designated herein as "DNA328133".

Figure 1906 shows the amino acid sequence (SEQ ID NO:1906) derived from the coding sequence of SEQ ID NO:1905 shown in Figure 1905.

Figure 1907 shows a nucleotide sequence (SEQ ID NO:1907) of a native sequence PRO84040 cDNA, wherein SEQ ID NO:1907 is a clone designated herein as "DNA328134".

5        Figure 1908 shows the amino acid sequence (SEQ ID NO:1908) derived from the coding sequence of SEQ ID NO:1907 shown in Figure 1907.

Figure 1909 shows a nucleotide sequence (SEQ ID NO:1909) of a native sequence PRO84041 cDNA, wherein SEQ ID NO:1909 is a clone designated herein as "DNA328135".

10       Figure 1910 shows the amino acid sequence (SEQ ID NO:1910) derived from the coding sequence of SEQ ID NO:1909 shown in Figure 1909.

Figure 1911 shows a nucleotide sequence (SEQ ID NO:1911) of a native sequence PRO84082 cDNA, wherein SEQ ID NO:1911 is a clone designated herein as "DNA328136".

Figure 1912 shows the amino acid sequence (SEQ ID NO:1912) derived from the coding sequence of SEQ ID NO:1911 shown in Figure 1911.

15       Figure 1913 shows a nucleotide sequence (SEQ ID NO:1913) of a native sequence PRQ45876 cDNA, wherein SEQ ID NO:1913 is a clone designated herein as "DNA210491".

Figure 1914 shows the amino acid sequence (SEQ ID NO:1914) derived from the coding sequence of SEQ ID NO:1913 shown in Figure 1913.

20       Figure 1915 shows a nucleotide sequence (SEQ ID NO:1915) of a native sequence PRO84043 cDNA, wherein SEQ ID NO:1915 is a clone designated herein as "DNA328137".

Figure 1916 shows the amino acid sequence (SEQ ID NO:1916) derived from the coding sequence of SEQ ID NO:1915 shown in Figure 1915.

Figure 1917 shows a nucleotide sequence (SEQ ID NO:1917) of a native sequence PRO84044 cDNA, wherein SEQ ID NO:1917 is a clone designated herein as "DNA328138".

25       Figure 1918 shows the amino acid sequence (SEQ ID NO:1918) derived from the coding sequence of SEQ ID NO:1917 shown in Figure 1917.

Figure 1919 shows a nucleotide sequence (SEQ ID NO:1919) of a native sequence PRO6006 cDNA, wherein SEQ ID NO:1919 is a clone designated herein as "DNA328139".

30       Figure 1920 shows the amino acid sequence (SEQ ID NO:1920) derived from the coding sequence of SEQ ID NO:1919 shown in Figure 1919.

Figure 1921 shows a nucleotide sequence (SEQ ID NO:1921) of a native sequence PRO84045 cDNA, wherein SEQ ID NO:1921 is a clone designated herein as "DNA328140".

Figure 1922 shows the amino acid sequence (SEQ ID NO:1922) derived from the coding sequence of SEQ ID NO:1921 shown in Figure 1921.

35       Figure 1923 shows a nucleotide sequence (SEQ ID NO:1923) of a native sequence PRO84046 cDNA, wherein SEQ ID NO:1923 is a clone designated herein as "DNA328141".

Figure 1924 shows the amino acid sequence (SEQ ID NO:1924) derived from the coding sequence of SEQ ID NO:1923 shown in Figure 1923.

40       Figure 1925 shows a nucleotide sequence (SEQ ID NO:1925) of a native sequence PRO84047 cDNA, wherein SEQ ID NO:1925 is a clone designated herein as "DNA328142".

Figure 1926 shows the amino acid sequence (SEQ ID NO:1926) derived from the coding sequence of SEQ ID NO:1925 shown in Figure 1925.

Figure 1927 shows a nucleotide sequence (SEQ ID NO:1927) of a native sequence PRO84048 cDNA, wherein SEQ ID NO:1927 is a clone designated herein as "DNA328143".

5        Figure 1928 shows the amino acid sequence (SEQ ID NO:1928) derived from the coding sequence of SEQ ID NO:1927 shown in Figure 1927.

Figure 1929 shows a nucleotide sequence (SEQ ID NO:1929) of a native sequence PRO84049 cDNA, wherein SEQ ID NO:1929 is a clone designated herein as "DNA328144".

10       Figure 1930 shows the amino acid sequence (SEQ ID NO:1930) derived from the coding sequence of SEQ ID NO:1929 shown in Figure 1929.

Figure 1931 shows a nucleotide sequence (SEQ ID NO:1931) of a native sequence PRO84050 cDNA, wherein SEQ ID NO:1931 is a clone designated herein as "DNA328145".

Figure 1932 shows the amino acid sequence (SEQ ID NO:1932) derived from the coding sequence of SEQ ID NO:1931 shown in Figure 1931.

15       Figure 1933 shows a nucleotide sequence (SEQ ID NO:1933) of a native sequence PRO84051 cDNA, wherein SEQ ID NO:1933 is a clone designated herein as "DNA328146".

Figure 1934 shows the amino acid sequence (SEQ ID NO:1934) derived from the coding sequence of SEQ ID NO:1933 shown in Figure 1933.

20       Figure 1935 shows a nucleotide sequence (SEQ ID NO:1935) of a native sequence PRO84052 cDNA, wherein SEQ ID NO:1935 is a clone designated herein as "DNA328147".

Figure 1936 shows the amino acid sequence (SEQ ID NO:1936) derived from the coding sequence of SEQ ID NO:1935 shown in Figure 1935.

Figure 1937 shows a nucleotide sequence (SEQ ID NO:1937) of a native sequence PRO84053 cDNA, wherein SEQ ID NO:1937 is a clone designated herein as "DNA328148".

25       Figure 1938 shows the amino acid sequence (SEQ ID NO:1938) derived from the coding sequence of SEQ ID NO:1937 shown in Figure 1937.

Figure 1939 shows a nucleotide sequence (SEQ ID NO:1939) of a native sequence PRO84054 cDNA, wherein SEQ ID NO:1939 is a clone designated herein as "DNA328149".

30       Figure 1940 shows the amino acid sequence (SEQ ID NO:1940) derived from the coding sequence of SEQ ID NO:1939 shown in Figure 1939.

Figure 1941 shows a nucleotide sequence (SEQ ID NO:1941) of a native sequence PRO1343 cDNA, wherein SEQ ID NO:1941 is a clone designated herein as "DNA66675".

Figure 1942 shows the amino acid sequence (SEQ ID NO:1942) derived from the coding sequence of SEQ ID NO:1941 shown in Figure 1941.

35       Figure 1943 shows a nucleotide sequence (SEQ ID NO:1943) of a native sequence PRO84055 cDNA, wherein SEQ ID NO:1943 is a clone designated herein as "DNA328150".

Figure 1944 shows the amino acid sequence (SEQ ID NO:1944) derived from the coding sequence of SEQ ID NO:1943 shown in Figure 1943.

40       Figure 1945 shows a nucleotide sequence (SEQ ID NO:1945) of a native sequence PRO84056 cDNA, wherein SEQ ID NO:1945 is a clone designated herein as "DNA328151".

Figure 1946 shows the amino acid sequence (SEQ ID NO:1946) derived from the coding sequence of SEQ ID NO:1945 shown in Figure 1945.

Figure 1947 shows a nucleotide sequence (SEQ ID NO:1947) of a native sequence PRO84057 cDNA, wherein SEQ ID NO:1947 is a clone designated herein as "DNA328152".

5        Figure 1948 shows the amino acid sequence (SEQ ID NO:1948) derived from the coding sequence of SEQ ID NO:1947 shown in Figure 1947.

Figure 1949 shows a nucleotide sequence (SEQ ID NO:1949) of a native sequence cDNA, wherein SEQ ID NO:1949 is a clone designated herein as "DNA257872".

10        Figure 1950 shows a nucleotide sequence (SEQ ID NO:1950) of a native sequence PRO84058 cDNA, wherein SEQ ID NO:1950 is a clone designated herein as "DNA328153".

Figure 1951 shows the amino acid sequence (SEQ ID NO:1951) derived from the coding sequence of SEQ ID NO:1950 shown in Figure 1950.

Figure 1952 shows a nucleotide sequence (SEQ ID NO:1952) of a native sequence PRO84059 cDNA, wherein SEQ ID NO:1952 is a clone designated herein as "DNA328154".

15        Figure 1953 shows the amino acid sequence (SEQ ID NO:1953) derived from the coding sequence of SEQ ID NO:1952 shown in Figure 1952.

Figure 1954 shows a nucleotide sequence (SEQ ID NO:1954) of a native sequence PRO84060 cDNA, wherein SEQ ID NO:1954 is a clone designated herein as "DNA328155".

20        Figure 1955 shows the amino acid sequence (SEQ ID NO:1955) derived from the coding sequence of SEQ ID NO:1954 shown in Figure 1954.

Figure 1956 shows a nucleotide sequence (SEQ ID NO:1956) of a native sequence PRO84061 cDNA, wherein SEQ ID NO:1956 is a clone designated herein as "DNA328156".

Figure 1957 shows the amino acid sequence (SEQ ID NO:1957) derived from the coding sequence of SEQ ID NO:1956 shown in Figure 1956.

25        Figure 1958 shows a nucleotide sequence (SEQ ID NO:1958) of a native sequence PRO84062 cDNA, wherein SEQ ID NO:1958 is a clone designated herein as "DNA328157".

Figure 1959 shows the amino acid sequence (SEQ ID NO:1959) derived from the coding sequence of SEQ ID NO:1958 shown in Figure 1958.

30        Figure 1960 shows a nucleotide sequence (SEQ ID NO:1960) of a native sequence PRO84063 cDNA, wherein SEQ ID NO:1960 is a clone designated herein as "DNA328158".

Figure 1961 shows the amino acid sequence (SEQ ID NO:1961) derived from the coding sequence of SEQ ID NO:1960 shown in Figure 1960.

Figure 1962 shows a nucleotide sequence (SEQ ID NO:1962) of a native sequence cDNA, wherein SEQ ID NO:1962 is a clone designated herein as "DNA328159".

35        Figure 1963 shows a nucleotide sequence (SEQ ID NO:1963) of a native sequence PRO84064 cDNA, wherein SEQ ID NO:1963 is a clone designated herein as "DNA328160".

Figure 1964 shows the amino acid sequence (SEQ ID NO:1964) derived from the coding sequence of SEQ ID NO:1963 shown in Figure 1963.

40        Figure 1965 shows a nucleotide sequence (SEQ ID NO:1965) of a native sequence PRO84065 cDNA, wherein SEQ ID NO:1965 is a clone designated herein as "DNA328161".



Figure 1966 shows the amino acid sequence (SEQ ID NO:1966) derived from the coding sequence of SEQ ID NO:1965 shown in Figure 1965.

Figure 1967 shows a nucleotide sequence (SEQ ID NO:1967) of a native sequence PRO84066 cDNA, wherein SEQ ID NO:1967 is a clone designated herein as "DNA328162".

5 Figure 1968 shows the amino acid sequence (SEQ ID NO:1968) derived from the coding sequence of SEQ ID NO:1967 shown in Figure 1967.

Figure 1969 shows a nucleotide sequence (SEQ ID NO:1969) of a native sequence PRO84067 cDNA, wherein SEQ ID NO:1969 is a clone designated herein as "DNA328163".

10 Figure 1970 shows the amino acid sequence (SEQ ID NO:1970) derived from the coding sequence of SEQ ID NO:1969 shown in Figure 1969.

Figure 1971 shows a nucleotide sequence (SEQ ID NO:1971) of a native sequence PRO84068 cDNA, wherein SEQ ID NO:1971 is a clone designated herein as "DNA328164".

Figure 1972 shows the amino acid sequence (SEQ ID NO:1972) derived from the coding sequence of SEQ ID NO:1971 shown in Figure 1971.

15 Figure 1973 shows a nucleotide sequence (SEQ ID NO:1973) of a native sequence PRO38220 cDNA, wherein SEQ ID NO:1973 is a clone designated herein as "DNA328165".

Figure 1974 shows the amino acid sequence (SEQ ID NO:1974) derived from the coding sequence of SEQ ID NO:1973 shown in Figure 1973.

20 Figure 1975 shows a nucleotide sequence (SEQ ID NO:1975) of a native sequence PRO84069 cDNA, wherein SEQ ID NO:1975 is a clone designated herein as "DNA328166".

Figure 1976 shows the amino acid sequence (SEQ ID NO:1976) derived from the coding sequence of SEQ ID NO:1975 shown in Figure 1975.

Figure 1977 shows a nucleotide sequence (SEQ ID NO:1977) of a native sequence PRO84070 cDNA, wherein SEQ ID NO:1977 is a clone designated herein as "DNA328167".

25 Figure 1978 shows the amino acid sequence (SEQ ID NO:1978) derived from the coding sequence of SEQ ID NO:1977 shown in Figure 1977.

Figure 1979 shows a nucleotide sequence (SEQ ID NO:1979) of a native sequence PRO84071 cDNA, wherein SEQ ID NO:1979 is a clone designated herein as "DNA328168".

30 Figure 1980 shows the amino acid sequence (SEQ ID NO:1980) derived from the coding sequence of SEQ ID NO:1979 shown in Figure 1979.

Figure 1981 shows a nucleotide sequence (SEQ ID NO:1981) of a native sequence PRO84072 cDNA, wherein SEQ ID NO:1981 is a clone designated herein as "DNA328169".

Figure 1982 shows the amino acid sequence (SEQ ID NO:1982) derived from the coding sequence of SEQ ID NO:1981 shown in Figure 1981.

35 Figure 1983 shows a nucleotide sequence (SEQ ID NO:1983) of a native sequence PRO84073 cDNA, wherein SEQ ID NO:1983 is a clone designated herein as "DNA328170".

Figure 1984 shows the amino acid sequence (SEQ ID NO:1984) derived from the coding sequence of SEQ ID NO:1983 shown in Figure 1983.

40 Figure 1985 shows a nucleotide sequence (SEQ ID NO:1985) of a native sequence PRO84074 cDNA, wherein SEQ ID NO:1985 is a clone designated herein as "DNA328171".

Figure 1986 shows the amino acid sequence (SEQ ID NO:1986) derived from the coding sequence of SEQ ID NO:1985 shown in Figure 1985.

Figure 1987 shows a nucleotide sequence (SEQ ID NO:1987) of a native sequence PRO84075 cDNA, wherein SEQ ID NO:1987 is a clone designated herein as "DNA328172".

5        Figure 1988 shows the amino acid sequence (SEQ ID NO:1988) derived from the coding sequence of SEQ ID NO:1987 shown in Figure 1987.

Figure 1989 shows a nucleotide sequence (SEQ ID NO:1989) of a native sequence PRO84076 cDNA, wherein SEQ ID NO:1989 is a clone designated herein as "DNA328173".

10       Figure 1990 shows the amino acid sequence (SEQ ID NO:1990) derived from the coding sequence of SEQ ID NO:1989 shown in Figure 1989.

Figure 1991 shows a nucleotide sequence (SEQ ID NO:1991) of a native sequence PRO84077 cDNA, wherein SEQ ID NO:1991 is a clone designated herein as "DNA328174".

Figure 1992 shows the amino acid sequence (SEQ ID NO:1992) derived from the coding sequence of SEQ ID NO:1991 shown in Figure 1991.

15       Figure 1993 shows a nucleotide sequence (SEQ ID NO:1993) of a native sequence PRO84078 cDNA, wherein SEQ ID NO:1993 is a clone designated herein as "DNA328175".

Figure 1994 shows the amino acid sequence (SEQ ID NO:1994) derived from the coding sequence of SEQ ID NO:1993 shown in Figure 1993.

20       Figure 1995 shows a nucleotide sequence (SEQ ID NO:1995) of a native sequence PRO84079 cDNA, wherein SEQ ID NO:1995 is a clone designated herein as "DNA328176".

Figure 1996 shows the amino acid sequence (SEQ ID NO:1996) derived from the coding sequence of SEQ ID NO:1995 shown in Figure 1995.

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Figure 1997 shows a nucleotide sequence (SEQ ID NO:1997) of a native sequence PRO84080 cDNA, wherein SEQ ID NO:1997 is a clone designated herein as "DNA328177".

25       Figure 1998 shows the amino acid sequence (SEQ ID NO:1998) derived from the coding sequence of SEQ ID NO:1997 shown in Figure 1997.

Figure 1999 shows a nucleotide sequence (SEQ ID NO:1999) of a native sequence PRO84081 cDNA, wherein SEQ ID NO:1999 is a clone designated herein as "DNA328178".

30       Figure 2000 shows the amino acid sequence (SEQ ID NO:2000) derived from the coding sequence of SEQ ID NO:1999 shown in Figure 1999.

Figure 2001 shows a nucleotide sequence (SEQ ID NO:2001) of a native sequence PRO84082 cDNA, wherein SEQ ID NO:2001 is a clone designated herein as "DNA328179".

Figure 2002 shows the amino acid sequence (SEQ ID NO:2002) derived from the coding sequence of SEQ ID NO:2001 shown in Figure 2001.

35       Figure 2003 shows a nucleotide sequence (SEQ ID NO:2003) of a native sequence PRO84083 cDNA, wherein SEQ ID NO:2003 is a clone designated herein as "DNA328180".

Figure 2004 shows the amino acid sequence (SEQ ID NO:2004) derived from the coding sequence of SEQ ID NO:2003 shown in Figure 2003.

40       Figure 2005 shows a nucleotide sequence (SEQ ID NO:2005) of a native sequence PRO84084 cDNA, wherein SEQ ID NO:2005 is a clone designated herein as "DNA328181".

Figure 2006 shows the amino acid sequence (SEQ ID NO:2006) derived from the coding sequence of SEQ ID NO:2005 shown in Figure 2005.

Figure 2007 shows a nucleotide sequence (SEQ ID NO:2007) of a native sequence PRO84085 cDNA, wherein SEQ ID NO:2007 is a clone designated herein as "DNA328182".

5        Figure 2008 shows the amino acid sequence (SEQ ID NO:2008) derived from the coding sequence of SEQ ID NO:2007 shown in Figure 2007.

Figure 2009 shows a nucleotide sequence (SEQ ID NO:2009) of a native sequence PRO84086 cDNA, wherein SEQ ID NO:2009 is a clone designated herein as "DNA328183".

10       Figure 2010 shows the amino acid sequence (SEQ ID NO:2010) derived from the coding sequence of SEQ ID NO:2009 shown in Figure 2009.

Figure 2011 shows a nucleotide sequence (SEQ ID NO:2011) of a native sequence PRO84087 cDNA, wherein SEQ ID NO:2011 is a clone designated herein as "DNA328184".

Figure 2012 shows the amino acid sequence (SEQ ID NO:2012) derived from the coding sequence of SEQ ID NO:2011 shown in Figure 2011.

15       Figure 2013 shows a nucleotide sequence (SEQ ID NO:2013) of a native sequence PRO52486 cDNA, wherein SEQ ID NO:2013 is a clone designated herein as "DNA257959".

Figure 2014 shows the amino acid sequence (SEQ ID NO:2014) derived from the coding sequence of SEQ ID NO:2013 shown in Figure 2013.

20       Figure 2015 shows a nucleotide sequence (SEQ ID NO:2015) of a native sequence PRO84088 cDNA, wherein SEQ ID NO:2015 is a clone designated herein as "DNA328185".

Figure 2016 shows the amino acid sequence (SEQ ID NO:2016) derived from the coding sequence of SEQ ID NO:2015 shown in Figure 2015.

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Figure 2017 shows a nucleotide sequence (SEQ ID NO:2017) of a native sequence PRO84089 cDNA, wherein SEQ ID NO:2017 is a clone designated herein as "DNA328186".

25       Figure 2018 shows the amino acid sequence (SEQ ID NO:2018) derived from the coding sequence of SEQ ID NO:2017 shown in Figure 2017.

Figure 2019 shows a nucleotide sequence (SEQ ID NO:2019) of a native sequence PRO84090 cDNA, wherein SEQ ID NO:2019 is a clone designated herein as "DNA328187".

30       Figure 2020 shows the amino acid sequence (SEQ ID NO:2020) derived from the coding sequence of SEQ ID NO:2019 shown in Figure 2019.

Figure 2021 shows a nucleotide sequence (SEQ ID NO:2021) of a native sequence PRO84091 cDNA, wherein SEQ ID NO:2021 is a clone designated herein as "DNA328188".

Figure 2022 shows the amino acid sequence (SEQ ID NO:2022) derived from the coding sequence of SEQ ID NO:2021 shown in Figure 2021.

35       Figure 2023 shows a nucleotide sequence (SEQ ID NO:2023) of a native sequence PRO84092 cDNA, wherein SEQ ID NO:2023 is a clone designated herein as "DNA328189".

Figure 2024 shows the amino acid sequence (SEQ ID NO:2024) derived from the coding sequence of SEQ ID NO:2023 shown in Figure 2023.

40       Figure 2025 shows a nucleotide sequence (SEQ ID NO:2025) of a native sequence PRO84093 cDNA, wherein SEQ ID NO:2025 is a clone designated herein as "DNA328190".

Figure 2026 shows the amino acid sequence (SEQ ID NO:2026) derived from the coding sequence of SEQ ID NO:2025 shown in Figure 2025.

Figure 2027 shows a nucleotide sequence (SEQ ID NO:2027) of a native sequence PRO84094 cDNA, wherein SEQ ID NO:2027 is a clone designated herein as "DNA328191".

5 Figure 2028 shows the amino acid sequence (SEQ ID NO:2028) derived from the coding sequence of SEQ ID NO:2027 shown in Figure 2027.

Figure 2029 shows a nucleotide sequence (SEQ ID NO:2029) of a native sequence PRO84095 cDNA, wherein SEQ ID NO:2029 is a clone designated herein as "DNA328192".

10 Figure 2030 shows the amino acid sequence (SEQ ID NO:2030) derived from the coding sequence of SEQ ID NO:2029 shown in Figure 2029.

Figure 2031 shows a nucleotide sequence (SEQ ID NO:2031) of a native sequence PRO84096 cDNA, wherein SEQ ID NO:2031 is a clone designated herein as "DNA328193".

Figure 2032 shows the amino acid sequence (SEQ ID NO:2032) derived from the coding sequence of SEQ ID NO:2031 shown in Figure 2031.

15 Figure 2033 shows a nucleotide sequence (SEQ ID NO:2033) of a native sequence PRO84097 cDNA, wherein SEQ ID NO:2033 is a clone designated herein as "DNA328194".

Figure 2034 shows the amino acid sequence (SEQ ID NO:2034) derived from the coding sequence of SEQ ID NO:2033 shown in Figure 2033.

20 Figure 2035 shows a nucleotide sequence (SEQ ID NO:2035) of a native sequence PRO84098 cDNA, wherein SEQ ID NO:2035 is a clone designated herein as "DNA328195".

Figure 2036 shows the amino acid sequence (SEQ ID NO:2036) derived from the coding sequence of SEQ ID NO:2035 shown in Figure 2035.

Figure 2037 shows a nucleotide sequence (SEQ ID NO:2037) of a native sequence PRO84099 cDNA, wherein SEQ ID NO:2037 is a clone designated herein as "DNA328196".

25 Figure 2038 shows the amino acid sequence (SEQ ID NO:2038) derived from the coding sequence of SEQ ID NO:2037 shown in Figure 2037.

Figure 2039 shows a nucleotide sequence (SEQ ID NO:2039) of a native sequence PRO84100 cDNA, wherein SEQ ID NO:2039 is a clone designated herein as "DNA328197".

30 Figure 2040 shows the amino acid sequence (SEQ ID NO:2040) derived from the coding sequence of SEQ ID NO:2039 shown in Figure 2039.

Figure 2041 shows a nucleotide sequence (SEQ ID NO:2041) of a native sequence PRO84101 cDNA, wherein SEQ ID NO:2041 is a clone designated herein as "DNA328198".

Figure 2042 shows the amino acid sequence (SEQ ID NO:2042) derived from the coding sequence of SEQ ID NO:2041 shown in Figure 2041.

35 Figure 2043 shows a nucleotide sequence (SEQ ID NO:2043) of a native sequence PRO84102 cDNA, wherein SEQ ID NO:2043 is a clone designated herein as "DNA328199".

Figure 2044 shows the amino acid sequence (SEQ ID NO:2044) derived from the coding sequence of SEQ ID NO:2043 shown in Figure 2043.

40 Figure 2045 shows a nucleotide sequence (SEQ ID NO:2045) of a native sequence PRO1274 cDNA, wherein SEQ ID NO:2045 is a clone designated herein as "DNA64889".

Figure 2046 shows the amino acid sequence (SEQ ID NO:2046) derived from the coding sequence of SEQ ID NO:2045 shown in Figure 2045.

Figure 2047 shows a nucleotide sequence (SEQ ID NO:2047) of a native sequence PRO84103 cDNA, wherein SEQ ID NO:2047 is a clone designated herein as "DNA328200".

5 Figure 2048 shows the amino acid sequence (SEQ ID NO:2048) derived from the coding sequence of SEQ ID NO:2047 shown in Figure 2047.

Figure 2049 shows a nucleotide sequence (SEQ ID NO:2049) of a native sequence PRO84104 cDNA, wherein SEQ ID NO:2049 is a clone designated herein as "DNA328201".

10 Figure 2050 shows the amino acid sequence (SEQ ID NO:2050) derived from the coding sequence of SEQ ID NO:2049 shown in Figure 2049.

Figure 2051 shows a nucleotide sequence (SEQ ID NO:2051) of a native sequence PRO69126 cDNA, wherein SEQ ID NO:2051 is a clone designated herein as "DNA285363".

Figure 2052 shows the amino acid sequence (SEQ ID NO:2052) derived from the coding sequence of SEQ ID NO:2051 shown in Figure 2051.

15 Figure 2053 shows a nucleotide sequence (SEQ ID NO:2053) of a native sequence PRO84105 cDNA, wherein SEQ ID NO:2053 is a clone designated herein as "DNA328202".

Figure 2054 shows the amino acid sequence (SEQ ID NO:2054) derived from the coding sequence of SEQ ID NO:2053 shown in Figure 2053.

20 Figure 2055 shows a nucleotide sequence (SEQ ID NO:2055) of a native sequence PRO84106 cDNA, wherein SEQ ID NO:2055 is a clone designated herein as "DNA328203".

Figure 2056 shows the amino acid sequence (SEQ ID NO:2056) derived from the coding sequence of SEQ ID NO:2055 shown in Figure 2055.

Figure 2057 shows a nucleotide sequence (SEQ ID NO:2057) of a native sequence PRO84107 cDNA, wherein SEQ ID NO:2057 is a clone designated herein as "DNA328204".

25 Figure 2058 shows the amino acid sequence (SEQ ID NO:2058) derived from the coding sequence of SEQ ID NO:2057 shown in Figure 2057.

Figure 2059 shows a nucleotide sequence (SEQ ID NO:2059) of a native sequence PRO84108 cDNA, wherein SEQ ID NO:2059 is a clone designated herein as "DNA328205".

30 Figure 2060 shows the amino acid sequence (SEQ ID NO:2060) derived from the coding sequence of SEQ ID NO:2059 shown in Figure 2059.

Figure 2061 shows a nucleotide sequence (SEQ ID NO:2061) of a native sequence PRO84109 cDNA, wherein SEQ ID NO:2061 is a clone designated herein as "DNA328206".

Figure 2062 shows the amino acid sequence (SEQ ID NO:2062) derived from the coding sequence of SEQ ID NO:2061 shown in Figure 2061.

35 Figure 2063 shows a nucleotide sequence (SEQ ID NO:2063) of a native sequence PRO84110 cDNA, wherein SEQ ID NO:2063 is a clone designated herein as "DNA328207".

Figure 2064 shows the amino acid sequence (SEQ ID NO:2064) derived from the coding sequence of SEQ ID NO:2063 shown in Figure 2063.

40 Figure 2065 shows a nucleotide sequence (SEQ ID NO:2065) of a native sequence PRO84111 cDNA, wherein SEQ ID NO:2065 is a clone designated herein as "DNA328208".

Figure 2066 shows the amino acid sequence (SEQ ID NO:2066) derived from the coding sequence of SEQ ID NO:2065 shown in Figure 2065.

Figure 2067 shows a nucleotide sequence (SEQ ID NO:2067) of a native sequence PRO84112 cDNA, wherein SEQ ID NO:2067 is a clone designated herein as "DNA328209".

5        Figure 2068 shows the amino acid sequence (SEQ ID NO:2068) derived from the coding sequence of SEQ ID NO:2067 shown in Figure 2067.

Figure 2069 shows a nucleotide sequence (SEQ ID NO:2069) of a native sequence PRO84113 cDNA, wherein SEQ ID NO:2069 is a clone designated herein as "DNA328210".

10       Figure 2070 shows the amino acid sequence (SEQ ID NO:2070) derived from the coding sequence of SEQ ID NO:2070 shown in Figure .

Figure 2071 shows a nucleotide sequence (SEQ ID NO:2071) of a native sequence PRO84114 cDNA, wherein SEQ ID NO:2071 is a clone designated herein as "DNA328211".

Figure 2072 shows the amino acid sequence (SEQ ID NO:2072) derived from the coding sequence of SEQ ID NO:2071 shown in Figure 2071.

15       Figure 2073 shows a nucleotide sequence (SEQ ID NO:2073) of a native sequence PRO84115 cDNA, wherein SEQ ID NO:2073 is a clone designated herein as "DNA328212".

Figure 2074 shows the amino acid sequence (SEQ ID NO:2074) derived from the coding sequence of SEQ ID NO:2073 shown in Figure 2073.

20       Figure 2075 shows a nucleotide sequence (SEQ ID NO:2075) of a native sequence PRO84116 cDNA, wherein SEQ ID NO:2075 is a clone designated herein as "DNA328213".

Figure 2076 shows the amino acid sequence (SEQ ID NO:2076) derived from the coding sequence of SEQ ID NO:2075 shown in Figure 2075.

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Figure 2077 shows a nucleotide sequence (SEQ ID NO:2077) of a native sequence PRO84117 cDNA, wherein SEQ ID NO:2077 is a clone designated herein as "DNA328214".

25       Figure 2078 shows the amino acid sequence (SEQ ID NO:2078) derived from the coding sequence of SEQ ID NO:2077 shown in Figure 2077.

Figure 2079 shows a nucleotide sequence (SEQ ID NO:2079) of a native sequence PRO84118 cDNA, wherein SEQ ID NO:2079 is a clone designated herein as "DNA328215".

30       Figure 2080 shows the amino acid sequence (SEQ ID NO:2080) derived from the coding sequence of SEQ ID NO:2079 shown in Figure 2079.

Figure 2081 shows a nucleotide sequence (SEQ ID NO:2081) of a native sequence PRO84119 cDNA, wherein SEQ ID NO:2081 is a clone designated herein as "DNA328216".

Figure 2082 shows the amino acid sequence (SEQ ID NO:2082) derived from the coding sequence of SEQ ID NO:2081 shown in Figure 2081.

35       Figure 2083 shows a nucleotide sequence (SEQ ID NO:2083) of a native sequence PRO84120 cDNA, wherein SEQ ID NO:2083 is a clone designated herein as "DNA328217".

Figure 2084 shows the amino acid sequence (SEQ ID NO:2084) derived from the coding sequence of SEQ ID NO:2083 shown in Figure 2083.

40       Figure 2085 shows a nucleotide sequence (SEQ ID NO:2085) of a native sequence PRO84121 cDNA, wherein SEQ ID NO:2085 is a clone designated herein as "DNA328218".

Figure 2086 shows the amino acid sequence (SEQ ID NO:2086) derived from the coding sequence of SEQ ID NO:2085 shown in Figure 2085.

Figure 2087 shows a nucleotide sequence (SEQ ID NO:2087) of a native sequence PRO84122 cDNA, wherein SEQ ID NO:2087 is a clone designated herein as "DNA328219".

5 Figure 2088 shows the amino acid sequence (SEQ ID NO:2088) derived from the coding sequence of SEQ ID NO:2087 shown in Figure 2087.

Figure 2089 shows a nucleotide sequence (SEQ ID NO:2089) of a native sequence PRO84123 cDNA, wherein SEQ ID NO:2089 is a clone designated herein as "DNA328220".

10 Figure 2090 shows the amino acid sequence (SEQ ID NO:2090) derived from the coding sequence of SEQ ID NO:2089 shown in Figure 2089.

Figure 2091 shows a nucleotide sequence (SEQ ID NO:2091) of a native sequence PRO84124 cDNA, wherein SEQ ID NO:2091 is a clone designated herein as "DNA328221".

Figure 2092 shows the amino acid sequence (SEQ ID NO:2092) derived from the coding sequence of SEQ ID NO:2091 shown in Figure 2091.

15 Figure 2093 shows a nucleotide sequence (SEQ ID NO:2093) of a native sequence PRO84125 cDNA, wherein SEQ ID NO:2093 is a clone designated herein as "DNA328222".

Figure 2094 shows the amino acid sequence (SEQ ID NO:2094) derived from the coding sequence of SEQ ID NO:2093 shown in Figure 2093.

20 Figure 2095 shows a nucleotide sequence (SEQ ID NO:2095) of a native sequence PRO84126 cDNA, wherein SEQ ID NO:2095 is a clone designated herein as "DNA328223".

Figure 2096 shows the amino acid sequence (SEQ ID NO:2096) derived from the coding sequence of SEQ ID NO:2095 shown in Figure 2095.

Figure 2097 shows a nucleotide sequence (SEQ ID NO:2097) of a native sequence PRO23265 cDNA, wherein SEQ ID NO:2097 is a clone designated herein as "DNA176718".

25 Figure 2098 shows the amino acid sequence (SEQ ID NO:2098) derived from the coding sequence of SEQ ID NO:2097 shown in Figure 2097.

Figure 2099 shows a nucleotide sequence (SEQ ID NO:2099) of a native sequence PRO84127 cDNA, wherein SEQ ID NO:2099 is a clone designated herein as "DNA328224".

30 Figure 2100 shows the amino acid sequence (SEQ ID NO:2100) derived from the coding sequence of SEQ ID NO:2099 shown in Figure 2099.

Figure 2101 shows a nucleotide sequence (SEQ ID NO:2101) of a native sequence PRO84128 cDNA, wherein SEQ ID NO:2101 is a clone designated herein as "DNA328225".

Figure 2102 shows the amino acid sequence (SEQ ID NO:2102) derived from the coding sequence of SEQ ID NO:2101 shown in Figure 2101.

35 Figure 2103 shows a nucleotide sequence (SEQ ID NO:2103) of a native sequence PRO84129 cDNA, wherein SEQ ID NO:2103 is a clone designated herein as "DNA328226".

Figure 2104 shows the amino acid sequence (SEQ ID NO:2104) derived from the coding sequence of SEQ ID NO:2103 shown in Figure 2103.

40 Figure 2105 shows a nucleotide sequence (SEQ ID NO:2105) of a native sequence PRO84130 cDNA, wherein SEQ ID NO:2105 is a clone designated herein as "DNA328227".

Figure 2106 shows the amino acid sequence (SEQ ID NO:2106) derived from the coding sequence of SEQ ID NO:2105 shown in Figure 2105.

Figure 2107 shows a nucleotide sequence (SEQ ID NO:2107) of a native sequence PRO84131 cDNA, wherein SEQ ID NO:2107 is a clone designated herein as "DNA328228".

5        Figure 2108 shows the amino acid sequence (SEQ ID NO:2108) derived from the coding sequence of SEQ ID NO:2107 shown in Figure 2107.

Figure 2109 shows a nucleotide sequence (SEQ ID NO:2109) of a native sequence PRO84132 cDNA, wherein SEQ ID NO:2109 is a clone designated herein as "DNA328229".

10       Figure 2110 shows the amino acid sequence (SEQ ID NO:2110) derived from the coding sequence of SEQ ID NO:2109 shown in Figure 2109.

Figure 2111 shows a nucleotide sequence (SEQ ID NO:2111) of a native sequence PRO84133 cDNA, wherein SEQ ID NO:2111 is a clone designated herein as "DNA328230".

Figure 2112 shows the amino acid sequence (SEQ ID NO:2112) derived from the coding sequence of SEQ ID NO:2111 shown in Figure 2111.

15       Figure 2113 shows a nucleotide sequence (SEQ ID NO:2113) of a native sequence PRO84134 cDNA, wherein SEQ ID NO:2113 is a clone designated herein as "DNA328231".

Figure 2114 shows the amino acid sequence (SEQ ID NO:2114) derived from the coding sequence of SEQ ID NO:2113 shown in Figure 2113.

20       Figure 2115 shows a nucleotide sequence (SEQ ID NO:2115) of a native sequence PRO84135 cDNA, wherein SEQ ID NO:2115 is a clone designated herein as "DNA328232".

Figure 2116 shows the amino acid sequence (SEQ ID NO:2116) derived from the coding sequence of SEQ ID NO:2115 shown in Figure 2115.

Figure 2117 shows a nucleotide sequence (SEQ ID NO:2117) of a native sequence PRO84136 cDNA, wherein SEQ ID NO:2117 is a clone designated herein as "DNA328233".

25       Figure 2118 shows the amino acid sequence (SEQ ID NO:2118) derived from the coding sequence of SEQ ID NO:2117 shown in Figure 2117.

Figure 2119 shows a nucleotide sequence (SEQ ID NO:2119) of a native sequence PRO84137 cDNA, wherein SEQ ID NO:2119 is a clone designated herein as "DNA328234".

30       Figure 2120 shows the amino acid sequence (SEQ ID NO:2120) derived from the coding sequence of SEQ ID NO:2119 shown in Figure 2119.

Figure 2121 shows a nucleotide sequence (SEQ ID NO:2121) of a native sequence PRO84138 cDNA, wherein SEQ ID NO:2121 is a clone designated herein as "DNA328235".

Figure 2122 shows the amino acid sequence (SEQ ID NO:2122) derived from the coding sequence of SEQ ID NO:2121 shown in Figure 2121.

35       Figure 2123 shows a nucleotide sequence (SEQ ID NO:2123) of a native sequence PRO84139 cDNA, wherein SEQ ID NO:2123 is a clone designated herein as "DNA328236".

Figure 2124 shows the amino acid sequence (SEQ ID NO:2124) derived from the coding sequence of SEQ ID NO:2123 shown in Figure 2123.

40       Figure 2125 shows a nucleotide sequence (SEQ ID NO:2125) of a native sequence PRO84140 cDNA, wherein SEQ ID NO:2125 is a clone designated herein as "DNA328237".



Figure 2126 shows the amino acid sequence (SEQ ID NO:2126) derived from the coding sequence of SEQ ID NO:2125 shown in Figure 2125.

Figure 2127 shows a nucleotide sequence (SEQ ID NO:2127) of a native sequence PRO84141 cDNA, wherein SEQ ID NO:2127 is a clone designated herein as "DNA328238".

5 Figure 2128 shows the amino acid sequence (SEQ ID NO:2128) derived from the coding sequence of SEQ ID NO:2127 shown in Figure 2127.

Figure 2129 shows a nucleotide sequence (SEQ ID NO:2129) of a native sequence PRO84142 cDNA, wherein SEQ ID NO:2129 is a clone designated herein as "DNA328239".

10 Figure 2130 shows the amino acid sequence (SEQ ID NO:2130) derived from the coding sequence of SEQ ID NO:2129 shown in Figure 2129.

Figure 2131 shows a nucleotide sequence (SEQ ID NO:2131) of a native sequence PRO84143 cDNA, wherein SEQ ID NO:2131 is a clone designated herein as "DNA328240".

Figure 2132 shows the amino acid sequence (SEQ ID NO:2132) derived from the coding sequence of SEQ ID NO:2131 shown in Figure 2131.

15 Figure 2133 shows a nucleotide sequence (SEQ ID NO:2133) of a native sequence PRO84144 cDNA, wherein SEQ ID NO:2133 is a clone designated herein as "DNA328241".

Figure 2134 shows the amino acid sequence (SEQ ID NO:2134) derived from the coding sequence of SEQ ID NO:2133 shown in Figure 2133.

20 Figure 2135 shows a nucleotide sequence (SEQ ID NO:2135) of a native sequence PRO84145 cDNA, wherein SEQ ID NO:2135 is a clone designated herein as "DNA328242".

Figure 2136 shows the amino acid sequence (SEQ ID NO:2136) derived from the coding sequence of SEQ ID NO:2135 shown in Figure 2135.

Figure 2137 shows a nucleotide sequence (SEQ ID NO:2137) of a native sequence cDNA, wherein SEQ ID NO:2137 is a clone designated herein as "DNA328243".

25 Figure 2138 shows a nucleotide sequence (SEQ ID NO:2138) of a native sequence PRO1889 cDNA, wherein SEQ ID NO:2138 is a clone designated herein as "DNA77623".

Figure 2139 shows the amino acid sequence (SEQ ID NO:2139) derived from the coding sequence of SEQ ID NO:2138 shown in Figure 2138.

30 Figure 2140 shows a nucleotide sequence (SEQ ID NO:2140) of a native sequence PRO1918 cDNA, wherein SEQ ID NO:2140 is a clone designated herein as "DNA328244".

Figure 2141 shows the amino acid sequence (SEQ ID NO:2141) derived from the coding sequence of SEQ ID NO:2140 shown in Figure 2140.

Figure 2142 shows a nucleotide sequence (SEQ ID NO:2142) of a native sequence PRO84146 cDNA, wherein SEQ ID NO:2142 is a clone designated herein as "DNA328245".

35 Figure 2143 shows the amino acid sequence (SEQ ID NO:2143) derived from the coding sequence of SEQ ID NO:2142 shown in Figure 2142.

Figure 2144 shows a nucleotide sequence (SEQ ID NO:2144) of a native sequence PRO83476 cDNA, wherein SEQ ID NO:2144 is a clone designated herein as "DNA327201".

40 Figure 2145 shows the amino acid sequence (SEQ ID NO:2145) derived from the coding sequence of SEQ ID NO:2144 shown in Figure 2144.

Figure 2146 shows a nucleotide sequence (SEQ ID NO:2146) of a native sequence cDNA, wherein SEQ ID NO:2146 is a clone designated herein as "DNA328246".

Figure 2147 shows a nucleotide sequence (SEQ ID NO:2147) of a native sequence cDNA, wherein SEQ ID NO:2147 is a clone designated herein as "DNA328247".

5        Figure 2148 shows a nucleotide sequence (SEQ ID NO:2148) of a native sequence PRO9871 cDNA, wherein SEQ ID NO:2148 is a clone designated herein as "DNA141423".

Figure 2149 shows the amino acid sequence (SEQ ID NO:2149) derived from the coding sequence of SEQ ID NO:2148 shown in Figure 2148.

10       Figure 2150 shows a nucleotide sequence (SEQ ID NO:2150) of a native sequence PRO19597 cDNA, wherein SEQ ID NO:2150 is a clone designated herein as "DNA143292".

Figure 2151 shows the amino acid sequence (SEQ ID NO:2151) derived from the coding sequence of SEQ ID NO:2150 shown in Figure 2150.

Figure 2152 shows a nucleotide sequence (SEQ ID NO:2152) of a native sequence PRO19600 cDNA, wherein SEQ ID NO:2152 is a clone designated herein as "DNA149876".

15       Figure 2153 shows the amino acid sequence (SEQ ID NO:2153) derived from the coding sequence of SEQ ID NO:2152 shown in Figure 2152.

Figure 2154 shows a nucleotide sequence (SEQ ID NO:2154) of a native sequence PRO28700 cDNA, wherein SEQ ID NO:2154 is a clone designated herein as "DNA176108".

20       Figure 2155 shows the amino acid sequence (SEQ ID NO:2155) derived from the coding sequence of SEQ ID NO:2154 shown in Figure 2154.

Figure 2156 shows a nucleotide sequence (SEQ ID NO:2156) of a native sequence PRO617 cDNA, wherein SEQ ID NO:2156 is a clone designated herein as "DNA48309".

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Figure 2157 shows the amino acid sequence (SEQ ID NO:2157) derived from the coding sequence of SEQ ID NO:2156 shown in Figure 2156.

25       Figure 2158 shows a nucleotide sequence (SEQ ID NO:2158) of a native sequence PRO844 cDNA, wherein SEQ ID NO:2158 is a clone designated herein as "DNA328248".

Figure 2159 shows the amino acid sequence (SEQ ID NO:2159) derived from the coding sequence of SEQ ID NO:2158 shown in Figure 2158.

30       Figure 2160 shows a nucleotide sequence (SEQ ID NO:2160) of a native sequence PRO71057 cDNA, wherein SEQ ID NO:2160 is a clone designated herein as "DNA304488".

Figure 2161 shows the amino acid sequence (SEQ ID NO:2161) derived from the coding sequence of SEQ ID NO:2160 shown in Figure 2160.

Figure 2162 shows a nucleotide sequence (SEQ ID NO:2162) of a native sequence PRO1160 cDNA, wherein SEQ ID NO:2162 is a clone designated herein as "DNA328249".

35       Figure 2163 shows the amino acid sequence (SEQ ID NO:2163) derived from the coding sequence of SEQ ID NO:2162 shown in Figure 2162.

Figure 2164 shows a nucleotide sequence (SEQ ID NO:2164) of a native sequence PRO1246 cDNA, wherein SEQ ID NO:2164 is a clone designated herein as "DNA64885".

40       Figure 2165 shows the amino acid sequence (SEQ ID NO:2165) derived from the coding sequence of SEQ ID NO:2164 shown in Figure 2164.

Figure 2166 shows a nucleotide sequence (SEQ ID NO:2166) of a native sequence PRO82061 cDNA, wherein SEQ ID NO:2166 is a clone designated herein as "DNA328250".

Figure 2167 shows the amino acid sequence (SEQ ID NO:2167) derived from the coding sequence of SEQ ID NO:2166 shown in Figure 2166.

5 Figure 2168 shows a nucleotide sequence (SEQ ID NO:2168) of a native sequence PRO84147 cDNA, wherein SEQ ID NO:2168 is a clone designated herein as "DNA328251".

Figure 2169 shows the amino acid sequence (SEQ ID NO:2169) derived from the coding sequence of SEQ ID NO:2168 shown in Figure 2168.

10 Figure 2170 shows a nucleotide sequence (SEQ ID NO:2170) of a native sequence PRO37534 cDNA, wherein SEQ ID NO:2170 is a clone designated herein as "DNA227071".

Figure 2171 shows the amino acid sequence (SEQ ID NO:2171) derived from the coding sequence of SEQ ID NO:2170 shown in Figure 2170.

Figure 2172 shows a nucleotide sequence (SEQ ID NO:2172) of a native sequence PRO84148 cDNA, wherein SEQ ID NO:2172 is a clone designated herein as "DNA328252".

15 Figure 2173 shows the amino acid sequence (SEQ ID NO:2173) derived from the coding sequence of SEQ ID NO:2172 shown in Figure 2172.

Figure 2174 shows a nucleotide sequence (SEQ ID NO:2174) of a native sequence PRO2561 cDNA, wherein SEQ ID NO:2174 is a clone designated herein as "DNA83020".

20 Figure 2175 shows the amino acid sequence (SEQ ID NO:2175) derived from the coding sequence of SEQ ID NO:2174 shown in Figure 2174.

Figure 2176 shows a nucleotide sequence (SEQ ID NO:2176) of a native sequence PRO37544 cDNA, wherein SEQ ID NO:2176 is a clone designated herein as "DNA227081".

Figure 2177 shows the amino acid sequence (SEQ ID NO:2177) derived from the coding sequence of SEQ ID NO:2176 shown in Figure 2176.

25 Figure 2178 shows a nucleotide sequence (SEQ ID NO:2178) of a native sequence PRO34252 cDNA, wherein SEQ ID NO:2178 is a clone designated herein as "DNA216500".

Figure 2179 shows the amino acid sequence (SEQ ID NO:2179) derived from the coding sequence of SEQ ID NO:2178 shown in Figure 2178.

30 Figure 2180 shows a nucleotide sequence (SEQ ID NO:2180) of a native sequence PRO84149 cDNA, wherein SEQ ID NO:2180 is a clone designated herein as "DNA328253".

Figure 2181 shows the amino acid sequence (SEQ ID NO:2181) derived from the coding sequence of SEQ ID NO:2180 shown in Figure 2180.

Figure 2182 shows a nucleotide sequence (SEQ ID NO:2182) of a native sequence PRO2763 cDNA, wherein SEQ ID NO:2182 is a clone designated herein as "DNA88359".

35 Figure 2183 shows the amino acid sequence (SEQ ID NO:2183) derived from the coding sequence of SEQ ID NO:2182 shown in Figure 2182.

Figure 2184 shows a nucleotide sequence (SEQ ID NO:2184) of a native sequence PRO11581 cDNA, wherein SEQ ID NO:2184 is a clone designated herein as "DNA328254".

40 Figure 2185 shows the amino acid sequence (SEQ ID NO:2185) derived from the coding sequence of SEQ ID NO:2184 shown in Figure 2184.

Figure 2186 shows a nucleotide sequence (SEQ ID NO:2186) of a native sequence PRO35988 cDNA, wherein SEQ ID NO:2186 is a clone designated herein as "DNA225525".

Figure 2187 shows the amino acid sequence (SEQ ID NO:2187) derived from the coding sequence of SEQ ID NO:2186 shown in Figure 2186.

5        Figure 2188 shows a nucleotide sequence (SEQ ID NO:2188) of a native sequence PRO34253 cDNA, wherein SEQ ID NO:2188 is a clone designated herein as "DNA216501".

Figure 2189 shows the amino acid sequence (SEQ ID NO:2189) derived from the coding sequence of SEQ ID NO:2188 shown in Figure 2188.

10       Figure 2190 shows a nucleotide sequence (SEQ ID NO:2190) of a native sequence PRO36305 cDNA, wherein SEQ ID NO:2190 is a clone designated herein as "DNA324774".

Figure 2191 shows the amino acid sequence (SEQ ID NO:2191) derived from the coding sequence of SEQ ID NO:2190 shown in Figure 2190.

Figure 2192 shows a nucleotide sequence (SEQ ID NO:2192) of a native sequence PRO36134 cDNA, wherein SEQ ID NO:2192 is a clone designated herein as "DNA225671".

15       Figure 2193 shows the amino acid sequence (SEQ ID NO:2193) derived from the coding sequence of SEQ ID NO:2192 shown in Figure 2192.

Figure 2194 shows a nucleotide sequence (SEQ ID NO:2194) of a native sequence PRO37076 cDNA, wherein SEQ ID NO:2194 is a clone designated herein as "DNA226613".

20       Figure 2195 shows the amino acid sequence (SEQ ID NO:2195) derived from the coding sequence of SEQ ID NO:2194 shown in Figure 2194.

Figure 2196 shows a nucleotide sequence (SEQ ID NO:2196) of a native sequence PRO84150 cDNA, wherein SEQ ID NO:2196 is a clone designated herein as "DNA228255".

Figure 2197 shows the amino acid sequence (SEQ ID NO:2197) derived from the coding sequence of SEQ ID NO:2196 shown in Figure 2196.

25       Figure 2198 shows a nucleotide sequence (SEQ ID NO:2198) of a native sequence PRO12564 cDNA, wherein SEQ ID NO:2198 is a clone designated herein as "DNA150971".

Figure 2199 shows the amino acid sequence (SEQ ID NO:2199) derived from the coding sequence of SEQ ID NO:2198 shown in Figure 2198.

30       Figure 2200 shows a nucleotide sequence (SEQ ID NO:2200) of a native sequence PRO2892 cDNA, wherein SEQ ID NO:2200 is a clone designated herein as "DNA88666".

Figure 2201 shows the amino acid sequence (SEQ ID NO:2201) derived from the coding sequence of SEQ ID NO:2200 shown in Figure 2200.

Figure 2202 shows a nucleotide sequence (SEQ ID NO:2202) of a native sequence PRO2712 cDNA, wherein SEQ ID NO:2202 is a clone designated herein as "DNA88240".

35       Figure 2203 shows the amino acid sequence (SEQ ID NO:2203) derived from the coding sequence of SEQ ID NO:2202 shown in Figure 2202.

Figure 2204 shows a nucleotide sequence (SEQ ID NO:2204) of a native sequence PRO2114 cDNA, wherein SEQ ID NO:2204 is a clone designated herein as "DNA328256".

40       Figure 2205 shows the amino acid sequence (SEQ ID NO:2205) derived from the coding sequence of SEQ ID NO:2204 shown in Figure 2204.

Figure 2206 shows a nucleotide sequence (SEQ ID NO:2206) of a native sequence PRO4815 cDNA, wherein SEQ ID NO:2206 is a clone designated herein as "DNA103488".

Figure 2207 shows the amino acid sequence (SEQ ID NO:2207) derived from the coding sequence of SEQ ID NO:2206 shown in Figure 2206.

5        Figure 2208 shows a nucleotide sequence (SEQ ID NO:2208) of a native sequence PRO11711 cDNA, wherein SEQ ID NO:2208 is a clone designated herein as "DNA151333".

Figure 2209 shows the amino acid sequence (SEQ ID NO:2209) derived from the coding sequence of SEQ ID NO:2208 shown in Figure 2208.

10       Figure 2210 shows a nucleotide sequence (SEQ ID NO:2210) of a native sequence PRO70862 cDNA, wherein SEQ ID NO:2210 is a clone designated herein as "DNA328257".

Figure 2211 shows the amino acid sequence (SEQ ID NO:2211) derived from the coding sequence of SEQ ID NO:2210 shown in Figure 2210.

Figure 2212 shows a nucleotide sequence (SEQ ID NO:2212) of a native sequence PRO21960 cDNA, wherein SEQ ID NO:2212 is a clone designated herein as "DNA192060".

15       Figure 2213 shows the amino acid sequence (SEQ ID NO:2213) derived from the coding sequence of SEQ ID NO:2212 shown in Figure 2212.

Figure 2214 shows a nucleotide sequence (SEQ ID NO:) of a native sequence PRO84151 cDNA, wherein SEQ ID NO:2214 is a clone designated herein as "DNA328258".

20       Figure 2215 shows the amino acid sequence (SEQ ID NO:2215) derived from the coding sequence of SEQ ID NO:2214 shown in Figure 2214.

Figure 2216 shows a nucleotide sequence (SEQ ID NO:2216) of a native sequence PRO2620 cDNA, wherein SEQ ID NO:2216 is a clone designated herein as "DNA328259".

Figure 2217A-B shows a nucleotide sequence (SEQ ID NO:2217) of a native sequence PRO62620 cDNA, wherein SEQ ID NO:2217 is a clone designated herein as "DNA83176".

25       Figure 2218 shows the amino acid sequence (SEQ ID NO:2218) derived from the coding sequence of SEQ ID NO:2217 shown in Figure 2217A-B.

Figure 2219 shows a nucleotide sequence (SEQ ID NO:2219) of a native sequence PRO37793 cDNA, wherein SEQ ID NO:2219 is a clone designated herein as "DNA227330".

30       Figure 2220 shows the amino acid sequence (SEQ ID NO:2220) derived from the coding sequence of SEQ ID NO:2219 shown in Figure 2219.

Figure 2221 shows a nucleotide sequence (SEQ ID NO:2221) of a native sequence PRO84152 cDNA, wherein SEQ ID NO:2221 is a clone designated herein as "DNA328260".

Figure 2222 shows the amino acid sequence (SEQ ID NO:2222) derived from the coding sequence of SEQ ID NO:2221 shown in Figure 2221.

35       Figure 2223 shows a nucleotide sequence (SEQ ID NO:2223) of a native sequence PRO37676 cDNA, wherein SEQ ID NO:2223 is a clone designated herein as "DNA227213".

Figure 2224 shows the amino acid sequence (SEQ ID NO:2224) derived from the coding sequence of SEQ ID NO:2223 shown in Figure 2223.

40       Figure 2225 shows a nucleotide sequence (SEQ ID NO:2225) of a native sequence PRO83477 cDNA, wherein SEQ ID NO:2225 is a clone designated herein as "DNA327204".

Figure 2226 shows the amino acid sequence (SEQ ID NO:2226) derived from the coding sequence of SEQ ID NO:2225 shown in Figure 2225.

Figure 2227 shows a nucleotide sequence (SEQ ID NO:2227) of a native sequence PRO37316 cDNA, wherein SEQ ID NO:2227 is a clone designated herein as "DNA226853".

5 Figure 2228 shows the amino acid sequence (SEQ ID NO:2228) derived from the coding sequence of SEQ ID NO:2227 shown in Figure 2227.

Figure 2229 shows a nucleotide sequence (SEQ ID NO:2229) of a native sequence cDNA, wherein SEQ ID NO:2229 is a clone designated herein as "DNA328261".

10 Figure 2230 shows a nucleotide sequence (SEQ ID NO:2230) of a native sequence PRO20129 cDNA, wherein SEQ ID NO: is a clone designated herein as "DNA171401".

Figure 2231 shows the amino acid sequence (SEQ ID NO:2231) derived from the coding sequence of SEQ ID NO:2230 shown in Figure 2230.

Figure 2232 shows a nucleotide sequence (SEQ ID NO:2232) of a native sequence PRO84153 cDNA, wherein SEQ ID NO:2232 is a clone designated herein as "DNA328262".

15 Figure 2233 shows the amino acid sequence (SEQ ID NO:2233) derived from the coding sequence of SEQ ID NO:2232 shown in Figure 2232.

Figure 2234 shows a nucleotide sequence (SEQ ID NO:2234) of a native sequence PRO4645 cDNA, wherein SEQ ID NO:2234 is a clone designated herein as "DNA328263".

20 Figure 2235 shows the amino acid sequence (SEQ ID NO:2235) derived from the coding sequence of SEQ ID NO:2234 shown in Figure 2234.

Figure 2236A-B shows a nucleotide sequence (SEQ ID NO:2236) of a native sequence PRO37137 cDNA, wherein ~~SEQ ID NO:2236 is a clone designated herein as "DNA226674".~~

Figure 2237 shows the amino acid sequence (SEQ ID NO:2237) derived from the coding sequence of SEQ ID NO:2236 shown in Figure 2236A-B.

25 Figure 2238 shows a nucleotide sequence (SEQ ID NO:2238) of a native sequence PRO36538 cDNA, wherein SEQ ID NO:2238 is a clone designated herein as "DNA226075".

Figure 2239 shows the amino acid sequence (SEQ ID NO:2239) derived from the coding sequence of SEQ ID NO:2238 shown in Figure 2238.

30 Figure 2240 shows a nucleotide sequence (SEQ ID NO:2240) of a native sequence PRO12087 cDNA, wherein SEQ ID NO:2240 is a clone designated herein as "DNA328264".

Figure 2241 shows the amino acid sequence (SEQ ID NO:2241) derived from the coding sequence of SEQ ID NO:2240 shown in Figure 2240.

Figure 2242 shows a nucleotide sequence (SEQ ID NO:2242) of a native sequence PRO4805 cDNA, wherein SEQ ID NO:2242 is a clone designated herein as "DNA103478".

35 Figure 2243 shows the amino acid sequence (SEQ ID NO:2243) derived from the coding sequence of SEQ ID NO:2242 shown in Figure 2242.

Figure 2244 shows a nucleotide sequence (SEQ ID NO:2244) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:2244 is a clone designated herein as "DNA328265".

40 Figure 2245 shows the amino acid sequence (SEQ ID NO:2245) derived from the coding sequence of SEQ ID NO:2244 shown in Figure 2244.

Figure 2246 shows a nucleotide sequence (SEQ ID NO:2246) of a native sequence PRO12125 cDNA, wherein SEQ ID NO:2246 is a clone designated herein as "DNA328266".

Figure 2247 shows the amino acid sequence (SEQ ID NO:2247) derived from the coding sequence of SEQ ID NO: 2246 shown in Figure 2246.

5        Figure 2248A-B shows a nucleotide sequence (SEQ ID NO:2248) of a native sequence PRO12864 cDNA, wherein SEQ ID NO:2248 is a clone designated herein as "DNA328267".

Figure 2249 shows the amino acid sequence (SEQ ID NO:2249) derived from the coding sequence of SEQ ID NO:2248 shown in Figure 2248A-B.

10       Figure 2250A-B shows a nucleotide sequence (SEQ ID NO:2250) of a native sequence PRO21704 cDNA, wherein SEQ ID NO:2250 is a clone designated herein as "DNA188192".

Figure 2251 shows the amino acid sequence (SEQ ID NO:2251) derived from the coding sequence of SEQ ID NO:2250 shown in Figure 2250A-B.

Figure 2252 shows a nucleotide sequence (SEQ ID NO:2252) of a native sequence PRO84154 cDNA, wherein SEQ ID NO:2252 is a clone designated herein as "DNA328268".

15       Figure 2253 shows the amino acid sequence (SEQ ID NO:2253) derived from the coding sequence of SEQ ID NO:2252 shown in Figure 2252.

Figure 2254 shows a nucleotide sequence (SEQ ID NO:2254) of a native sequence PRO2115 cDNA, wherein SEQ ID NO:2254 is a clone designated herein as "DNA328269".

20       Figure 2255 shows the amino acid sequence (SEQ ID NO:2255) derived from the coding sequence of SEQ ID NO:2254 shown in Figure 2254.

Figure 2256 shows a nucleotide sequence (SEQ ID NO:2256) of a native sequence PRO4583 cDNA, wherein SEQ ID NO:2256 is a clone designated herein as "DNA103253".

Figure 2257 shows the amino acid sequence (SEQ ID NO:2257) derived from the coding sequence of SEQ ID NO:2256 shown in Figure 2256.

25       Figure 2258 shows a nucleotide sequence (SEQ ID NO:2258) of a native sequence PRO118 cDNA, wherein SEQ ID NO:2258 is a clone designated herein as "DNA52749".

Figure 2259 shows the amino acid sequence (SEQ ID NO:2259) derived from the coding sequence of SEQ ID NO:2258 shown in Figure 2258.

30       Figure 2260 shows a nucleotide sequence (SEQ ID NO:2260) of a native sequence PRO69926 cDNA, wherein SEQ ID NO:2260 is a clone designated herein as "DNA287951".

Figure 2261 shows the amino acid sequence (SEQ ID NO:2261) derived from the coding sequence of SEQ ID NO:2260 shown in Figure 2260.

Figure 2262 shows a nucleotide sequence (SEQ ID NO:2262) of a native sequence PRO38180 cDNA, wherein SEQ ID NO:2262 is a clone designated herein as "DNA227717".

35       Figure 2263 shows the amino acid sequence (SEQ ID NO:2263) derived from the coding sequence of SEQ ID NO:2262 shown in Figure 2262.

Figure 2264 shows a nucleotide sequence (SEQ ID NO:2264) of a native sequence PRO9901 cDNA, wherein SEQ ID NO:2264 is a clone designated herein as "DNA328270".

40       Figure 2265 shows the amino acid sequence (SEQ ID NO:2265) derived from the coding sequence of SEQ ID NO:2264 shown in Figure 2264.

Figure 2266 shows a nucleotide sequence (SEQ ID NO:2266) of a native sequence PRO81868 cDNA, wherein SEQ ID NO:2266 is a clone designated herein as "DNA328271".

Figure 2267 shows the amino acid sequence (SEQ ID NO:2267) derived from the coding sequence of SEQ ID NO:2266 shown in Figure 2266.

5        Figure 2268 shows a nucleotide sequence (SEQ ID NO:2268) of a native sequence PRO36024 cDNA, wherein SEQ ID NO:2268 is a clone designated herein as "DNA225561".

Figure 2269 shows the amino acid sequence (SEQ ID NO:2269) derived from the coding sequence of SEQ ID NO:2268 shown in Figure 2268.

10       Figure 2270 shows a nucleotide sequence (SEQ ID NO:2270) of a native sequence PRO70976 cDNA, wherein SEQ ID NO:2270 is a clone designated herein as "DNA328272".

Figure 2271 shows the amino acid sequence (SEQ ID NO:2271) derived from the coding sequence of SEQ ID NO:2270 shown in Figure 2270.

Figure 2272 shows a nucleotide sequence (SEQ ID NO:2272) of a native sequence PRO23248 cDNA, wherein SEQ ID NO:2272 is a clone designated herein as "DNA325110".

15       Figure 2273 shows the amino acid sequence (SEQ ID NO:2273) derived from the coding sequence of SEQ ID NO: 2272 shown in Figure 2272.

Figure 2274 shows a nucleotide sequence (SEQ ID NO:2274) of a native sequence PRO84155 cDNA, wherein SEQ ID NO:2274 is a clone designated herein as "DNA328273".

20       Figure 2275 shows the amino acid sequence (SEQ ID NO:2275) derived from the coding sequence of SEQ ID NO:2274 shown in Figure 2274.

Figure 2276 shows a nucleotide sequence (SEQ ID NO:2276) of a native sequence PRO33683 cDNA, wherein SEQ ID NO:2276 is a clone designated herein as "DNA210138".

Figure 2277 shows the amino acid sequence (SEQ ID NO:2277) derived from the coding sequence of SEQ ID NO:2276 shown in Figure 2276.

25       Figure 2278A-B shows a nucleotide sequence (SEQ ID NO:2278) of a native sequence PRO37368 cDNA, wherein SEQ ID NO:2278 is a clone designated herein as "DNA226905".

Figure 2279 shows the amino acid sequence (SEQ ID NO:2279) derived from the coding sequence of SEQ ID NO:2278 shown in Figure 2278A-B.

30       Figure 2280 shows a nucleotide sequence (SEQ ID NO:2280) of a native sequence PRO12912 cDNA, wherein SEQ ID NO:2280 is a clone designated herein as "DNA328274".

Figure 2281 shows the amino acid sequence (SEQ ID NO:2281) derived from the coding sequence of SEQ ID NO:2280 shown in Figure 2280.

Figure 2282 shows a nucleotide sequence (SEQ ID NO:2282) of a native sequence PRO12752 cDNA, wherein SEQ ID NO:2282 is a clone designated herein as "DNA151907".

35       Figure 2283 shows the amino acid sequence (SEQ ID NO:2283) derived from the coding sequence of SEQ ID NO:2282 shown in Figure 2282.

Figure 2284 shows a nucleotide sequence (SEQ ID NO:2284) of a native sequence PRO21687 cDNA, wherein SEQ ID NO:2284 is a clone designated herein as "DNA188181".

40       Figure 2285 shows the amino acid sequence (SEQ ID NO:2285) derived from the coding sequence of SEQ ID NO:2284 shown in Figure 2284.



Figure 2286 shows a nucleotide sequence (SEQ ID NO:2286) of a native sequence PRO200 cDNA, wherein SEQ ID NO:2286 is a clone designated herein as "DNA327202".

Figure 2287 shows the amino acid sequence (SEQ ID NO:2287) derived from the coding sequence of SEQ ID NO:2286 shown in Figure 2286.

5        Figure 2288 shows a nucleotide sequence (SEQ ID NO:2288) of a native sequence PRO36003 cDNA, wherein SEQ ID NO:2288 is a clone designated herein as "DNA225540".

Figure 2289 shows the amino acid sequence (SEQ ID NO:2289) derived from the coding sequence of SEQ ID NO:2288 shown in Figure 2288.

10       Figure 2290 shows a nucleotide sequence (SEQ ID NO:2290) of a native sequence PRO84156 cDNA, wherein SEQ ID NO:2290 is a clone designated herein as "DNA328275".

Figure 2291 shows the amino acid sequence (SEQ ID NO:2291) derived from the coding sequence of SEQ ID NO:2290 shown in Figure 2290.

Figure 2292 shows a nucleotide sequence (SEQ ID NO:2292) of a native sequence PRO84157 cDNA, wherein SEQ ID NO:2292 is a clone designated herein as "DNA328276".

15       Figure 2293 shows the amino acid sequence (SEQ ID NO:2293) derived from the coding sequence of SEQ ID NO:2292 shown in Figure 2292.

Figure 2294 shows a nucleotide sequence (SEQ ID NO:2294) of a native sequence PRO36079 cDNA, wherein SEQ ID NO:2294 is a clone designated herein as "DNA328277".

20       Figure 2295 shows the amino acid sequence (SEQ ID NO:2295) derived from the coding sequence of SEQ ID NO:2294 shown in Figure 2294.

Figure 2296A-B shows a nucleotide sequence (SEQ ID NO:2296) of a native sequence PRO12450 cDNA, wherein SEQ ID NO:2296 is a clone designated herein as "DNA328278".

Figure 2297 shows the amino acid sequence (SEQ ID NO:2297) derived from the coding sequence of SEQ ID NO:2296 shown in Figure 2296A-B

25       Figure 2298 shows a nucleotide sequence (SEQ ID NO:2298) of a native sequence PRO83475 cDNA, wherein SEQ ID NO:2298 is a clone designated herein as "DNA327199".

Figure 2299 shows the amino acid sequence (SEQ ID NO:2299) derived from the coding sequence of SEQ ID NO:2298 shown in Figure 2298.

30       Figure 2300 shows a nucleotide sequence (SEQ ID NO:2300) of a native sequence cDNA, wherein SEQ ID NO:2300 is a clone designated herein as "DNA328279".

Figure 2301 shows a nucleotide sequence (SEQ ID NO:2301) of a native sequence PRO1213 cDNA, wherein SEQ ID NO:2301 is a clone designated herein as "DNA66487".

Figure 2302 shows the amino acid sequence (SEQ ID NO:2302) derived from the coding sequence of SEQ ID NO:2301 shown in Figure 2301.

35       Figure 2303 shows a nucleotide sequence (SEQ ID NO:2303) of a native sequence PRO82992 cDNA, wherein SEQ ID NO:2303 is a clone designated herein as "DNA326639".

Figure 2304 shows the amino acid sequence (SEQ ID NO:2304) derived from the coding sequence of SEQ ID NO:2303 shown in Figure 2303.

40       Figure 2305A-B shows a nucleotide sequence (SEQ ID NO:2305) of a native sequence PRO38492 cDNA, wherein SEQ ID NO:2305 is a clone designated herein as "DNA228029".

Figure 2306 shows the amino acid sequence (SEQ ID NO:2306) derived from the coding sequence of SEQ ID NO:2305 shown in Figure 2305A-B.

Figure 2307 shows a nucleotide sequence (SEQ ID NO:2307) of a native sequence cDNA, wherein SEQ ID NO:2307 is a clone designated herein as "DNA150981".

5        Figure 2308 shows a nucleotide sequence (SEQ ID NO:2308) of a native sequence cDNA, wherein SEQ ID NO:2308 is a clone designated herein as "DNA154390".

Figure 2309A-B shows a nucleotide sequence (SEQ ID NO:2309) of a native sequence PRO84158 cDNA, wherein SEQ ID NO:2309 is a clone designated herein as "DNA328280".

10       Figure 2310 shows the amino acid sequence (SEQ ID NO:2310) derived from the coding sequence of SEQ ID NO:2309 shown in Figure 2309A-B.

Figure 2311 shows a nucleotide sequence (SEQ ID NO:2311) of a native sequence cDNA, wherein SEQ ID NO:2311 is a clone designated herein as "DNA328281".

Figure 2312 shows a nucleotide sequence (SEQ ID NO:2312) of a native sequence PRO11738 cDNA, wherein SEQ ID NO:2312 is a clone designated herein as "DNA151360".

15       Figure 2313 shows the amino acid sequence (SEQ ID NO:2313) derived from the coding sequence of SEQ ID NO:2312 shown in Figure 2312.

Figure 2314 shows a nucleotide sequence (SEQ ID NO:2314) of a native sequence PRO11820 cDNA, wherein SEQ ID NO:2314 is a clone designated herein as "DNA151466".

20       Figure 2315 shows the amino acid sequence (SEQ ID NO:2315) derived from the coding sequence of SEQ ID NO:2314 shown in Figure 2314.

Figure 2316 shows a nucleotide sequence (SEQ ID NO:2316) of a native sequence PRO11863 cDNA, wherein SEQ ID NO:2316 is a clone designated herein as "DNA151518".

Figure 2317 shows the amino acid sequence (SEQ ID NO:2317) derived from the coding sequence of SEQ ID NO:2316 shown in Figure 2316.

25       Figure 2318A-B shows a nucleotide sequence (SEQ ID NO:2318) of a native sequence PRO84159 cDNA, wherein SEQ ID NO:2318 is a clone designated herein as "DNA328282".

Figure 2319 shows the amino acid sequence (SEQ ID NO:2319) derived from the coding sequence of SEQ ID NO:2318 shown in Figure 2319A-B.

30       Figure 2320 shows a nucleotide sequence (SEQ ID NO:2320) of a native sequence PRO11899 cDNA, wherein SEQ ID NO:2320 is a clone designated herein as "DNA151578".

Figure 2321 shows the amino acid sequence (SEQ ID NO:2321) derived from the coding sequence of SEQ ID NO:2320 shown in Figure 2320.

Figure 2322A-B shows a nucleotide sequence (SEQ ID NO:2322) of a native sequence cDNA, wherein SEQ ID NO:2322 is a clone designated herein as "DNA328283".

35       Figure 2323A-B shows a nucleotide sequence (SEQ ID NO:2323) of a native sequence PRO84160 cDNA, wherein SEQ ID NO:2323 is a clone designated herein as "DNA328284".

Figure 2324 shows the amino acid sequence (SEQ ID NO:2324) derived from the coding sequence of SEQ ID NO:2323 shown in Figure 2323A-B.

40       Figure 2325 shows a nucleotide sequence (SEQ ID NO:2325) of a native sequence PRO12039 cDNA, wherein SEQ ID NO:2325 is a clone designated herein as "DNA151761".

Figure 2326 shows the amino acid sequence (SEQ ID NO:2326) derived from the coding sequence of SEQ ID NO:2325 shown in Figure 2325.

Figure 2327 shows a nucleotide sequence (SEQ ID NO:2327) of a native sequence PRO12052 cDNA, wherein SEQ ID NO:2327 is a clone designated herein as "DNA151774".

5        Figure 2328 shows the amino acid sequence (SEQ ID NO:2328) derived from the coding sequence of SEQ ID NO:2327 shown in Figure 2327.

Figure 2329 shows a nucleotide sequence (SEQ ID NO:2329) of a native sequence PRO84161 cDNA, wherein SEQ ID NO:2329 is a clone designated herein as "DNA328285".

10       Figure 2330 shows the amino acid sequence (SEQ ID NO:2330) derived from the coding sequence of SEQ ID NO:2329 shown in Figure 2329.

Figure 2331A-B shows a nucleotide sequence (SEQ ID NO:2331) of a native sequence PRO69594 cDNA, wherein SEQ ID NO:2331 is a clone designated herein as "DNA287330".

Figure 2332 shows the amino acid sequence (SEQ ID NO:2332) derived from the coding sequence of SEQ ID NO:2331 shown in Figure 2331A-B.

15       Figure 2333 shows a nucleotide sequence (SEQ ID NO:2333) of a native sequence PRO84162 cDNA, wherein SEQ ID NO:2333 is a clone designated herein as "DNA328286".

Figure 2334 shows the amino acid sequence (SEQ ID NO:2334) derived from the coding sequence of SEQ ID NO:2333 shown in Figure 2333.

20       Figure 2335 shows a nucleotide sequence (SEQ ID NO:2335) of a native sequence PRO23605 cDNA, wherein SEQ ID NO:2335 is a clone designated herein as "DNA194213".

Figure 2336 shows the amino acid sequence (SEQ ID NO:2336) derived from the coding sequence of SEQ ID NO:2335 shown in Figure 2335.

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Figure 2337 shows a nucleotide sequence (SEQ ID NO:2337) of a native sequence PRO23896 cDNA, wherein SEQ ID NO:2337 is a clone designated herein as "DNA194541".

25       Figure 2338 shows the amino acid sequence (SEQ ID NO:2338) derived from the coding sequence of SEQ ID NO:2337 shown in Figure 2337.

Figure 2339A-B shows a nucleotide sequence (SEQ ID NO:2339) of a native sequence PRO24103 cDNA, wherein SEQ ID NO:2339 is a clone designated herein as "DNA194840".

30       Figure 2340 shows the amino acid sequence (SEQ ID NO:2340) derived from the coding sequence of SEQ ID NO:2339 shown in Figure 2339A-B.

Figure 2341A-C shows a nucleotide sequence (SEQ ID NO:2341) of a native sequence PRO84163 cDNA, wherein SEQ ID NO:2341 is a clone designated herein as "DNA328287".

Figure 2342 shows the amino acid sequence (SEQ ID NO:2342) derived from the coding sequence of SEQ ID NO:2341 shown in Figure 2341A-C.

35       Figure 2343 shows a nucleotide sequence (SEQ ID NO:2343) of a native sequence PRO69876 cDNA, wherein SEQ ID NO:2343 is a clone designated herein as "DNA328288".

Figure 2344 shows the amino acid sequence (SEQ ID NO:2344) derived from the coding sequence of SEQ ID NO:2343 shown in Figure 2343.

40       Figure 2345 shows a nucleotide sequence (SEQ ID NO:2345) of a native sequence cDNA, wherein SEQ ID NO:2345 is a clone designated herein as "DNA196275".

Figure 2346 shows a nucleotide sequence (SEQ ID NO:2346) of a native sequence PRO28564 cDNA, wherein SEQ ID NO:2346 is a clone designated herein as "DNA199066".

Figure 2347 shows the amino acid sequence (SEQ ID NO:2347) derived from the coding sequence of SEQ ID NO:2346 shown in Figure 2346.

5        Figure 2348 shows a nucleotide sequence (SEQ ID NO:2348) of a native sequence cDNA, wherein SEQ ID NO:2348 is a clone designated herein as "DNA328289".

Figure 2349 shows a nucleotide sequence (SEQ ID NO:2349) of a native sequence PRO33767 cDNA, wherein SEQ ID NO:2349 is a clone designated herein as "DNA210233".

10       Figure 2350 shows the amino acid sequence (SEQ ID NO:2350) derived from the coding sequence of SEQ ID NO:2349 shown in Figure 2349.

Figure 2351 shows a nucleotide sequence (SEQ ID NO:2351) of a native sequence PRO84164 cDNA, wherein SEQ ID NO:2351 is a clone designated herein as "DNA328290".

Figure 2352 shows the amino acid sequence (SEQ ID NO:2352) derived from the coding sequence of SEQ ID NO:2351 shown in Figure 2351.

15       Figure 2353A-B shows a nucleotide sequence (SEQ ID NO:2353) of a native sequence PRO19724 cDNA, wherein SEQ ID NO:2353 is a clone designated herein as "DNA73873".

Figure 2354 shows the amino acid sequence (SEQ ID NO:2354) derived from the coding sequence of SEQ ID NO:2353 shown in Figure 2353A-B.

20       Figure 2355A-C shows a nucleotide sequence (SEQ ID NO:2355) of a native sequence PRO84165 cDNA, wherein SEQ ID NO:2355 is a clone designated herein as "DNA328291".

Figure 2356 shows the amino acid sequence (SEQ ID NO:2356) derived from the coding sequence of SEQ ID NO:2355 shown in Figure 2355A-C.

Figure 2357 shows a nucleotide sequence (SEQ ID NO:2357) of a native sequence PRO84166 cDNA, wherein SEQ ID NO:2357 is a clone designated herein as "DNA328292".

25       Figure 2358 shows the amino acid sequence (SEQ ID NO:2358) derived from the coding sequence of SEQ ID NO:2357 shown in Figure 2357.

Figure 2359 shows a nucleotide sequence (SEQ ID NO:2359) of a native sequence PRO63135 cDNA, wherein SEQ ID NO:2359 is a clone designated herein as "DNA328293".

30       Figure 2360 shows the amino acid sequence (SEQ ID NO:2360) derived from the coding sequence of SEQ ID NO:2359 shown in Figure 2359.

Figure 2361 shows a nucleotide sequence (SEQ ID NO:2361) of a native sequence PRO58823 cDNA, wherein SEQ ID NO:2361 is a clone designated herein as "DNA270444".

Figure 2362 shows the amino acid sequence (SEQ ID NO:2362) derived from the coding sequence of SEQ ID NO:2361 shown in Figure 2361.

35       Figure 2363 shows a nucleotide sequence (SEQ ID NO:2363) of a native sequence PRO51466 cDNA, wherein SEQ ID NO:2363 is a clone designated herein as "DNA256405".

Figure 2364 shows the amino acid sequence (SEQ ID NO:2364) derived from the coding sequence of SEQ ID NO:2363 shown in Figure 2363.

40       Figure 2365 shows a nucleotide sequence (SEQ ID NO:2365) of a native sequence PRO51081 cDNA, wherein SEQ ID NO:2365 is a clone designated herein as "DNA256033".

Figure 2366 shows the amino acid sequence (SEQ ID NO:2366) derived from the coding sequence of SEQ ID NO:2365 shown in Figure 2365.

Figure 2367 shows a nucleotide sequence (SEQ ID NO:2367) of a native sequence PRO49244 cDNA, wherein SEQ ID NO:2367 is a clone designated herein as "DNA254129".

5        Figure 2368 shows the amino acid sequence (SEQ ID NO:2368) derived from the coding sequence of SEQ ID NO:2367 shown in Figure 2367.

Figure 2369 shows a nucleotide sequence (SEQ ID NO:2369) of a native sequence PRO84167 cDNA, wherein SEQ ID NO:2369 is a clone designated herein as "DNA328294".

10       Figure 2370 shows the amino acid sequence (SEQ ID NO:2370) derived from the coding sequence of SEQ ID NO:2369 shown in Figure 2396.

Figure 2371 shows a nucleotide sequence (SEQ ID NO:2371) of a native sequence PRO49824 cDNA, wherein SEQ ID NO:2371 is a clone designated herein as "DNA254725".

Figure 2372 shows the amino acid sequence (SEQ ID NO:2372) derived from the coding sequence of SEQ ID NO:2371 shown in Figure 2371.

15       Figure 2373 shows a nucleotide sequence (SEQ ID NO:2373) of a native sequence PRO84168 cDNA, wherein SEQ ID NO:2373 is a clone designated herein as "DNA328295".

Figure 2374 shows the amino acid sequence (SEQ ID NO:2374) derived from the coding sequence of SEQ ID NO:2373 shown in Figure 2373.

20       Figure 2375 shows a nucleotide sequence (SEQ ID NO:2375) of a native sequence PRO51817 cDNA, wherein SEQ ID NO:2375 is a clone designated herein as "DNA328296".

Figure 2376 shows the amino acid sequence (SEQ ID NO:2376) derived from the coding sequence of SEQ ID NO:2375 shown in Figure 2375.

Figure 2377 shows a nucleotide sequence (SEQ ID NO:2377) of a native sequence PRO59418 cDNA, wherein SEQ ID NO:2377 is a clone designated herein as "DNA328297".

25       Figure 2378 shows the amino acid sequence (SEQ ID NO:2378) derived from the coding sequence of SEQ ID NO:2377 shown in Figure 2377.

Figure 2379 shows a nucleotide sequence (SEQ ID NO:2379) of a native sequence PRO84169 cDNA, wherein SEQ ID NO:2379 is a clone designated herein as "DNA328298".

30       Figure 2380 shows the amino acid sequence (SEQ ID NO:2380) derived from the coding sequence of SEQ ID NO:2379 shown in Figure 2379.

Figure 2381 shows a nucleotide sequence (SEQ ID NO:2381) of a native sequence PRO132 cDNA, wherein SEQ ID NO:2381 is a clone designated herein as "DNA53532".

Figure 2382 shows the amino acid sequence (SEQ ID NO:2382) derived from the coding sequence of SEQ ID NO:2381 shown in Figure 2381.

35       Figure 2383 shows a nucleotide sequence (SEQ ID NO:2383) of a native sequence PRO51331 cDNA, wherein SEQ ID NO:2383 is a clone designated herein as "DNA256287".

Figure 2384 shows the amino acid sequence (SEQ ID NO:2384) derived from the coding sequence of SEQ ID NO:2383 shown in Figure 2383.

40       Figure 2385 shows a nucleotide sequence (SEQ ID NO:2385) of a native sequence PRO50371 cDNA, wherein SEQ ID NO:2385 is a clone designated herein as "DNA255298".

Figure 2386 shows the amino acid sequence (SEQ ID NO:2386) derived from the coding sequence of SEQ ID NO:2385 shown in Figure 2385.

Figure 2387 shows a nucleotide sequence (SEQ ID NO:2387) of a native sequence PRO84170 cDNA, wherein SEQ ID NO:2387 is a clone designated herein as "DNA328299".

5        Figure 2388 shows the amino acid sequence (SEQ ID NO:2388) derived from the coding sequence of SEQ ID NO:2387 shown in Figure 2387.

Figure 2389 shows a nucleotide sequence (SEQ ID NO:2389) of a native sequence PRO84171 cDNA, wherein SEQ ID NO:2389 is a clone designated herein as "DNA328300".

10       Figure 2390 shows the amino acid sequence (SEQ ID NO:2390) derived from the coding sequence of SEQ ID NO:2389 shown in Figure 2389.

Figure 2391 shows a nucleotide sequence (SEQ ID NO:2391) of a native sequence PRO70371 cDNA, wherein SEQ ID NO:2391 is a clone designated herein as "DNA328301".

Figure 2392 shows the amino acid sequence (SEQ ID NO:2392) derived from the coding sequence of SEQ ID NO:2391 shown in Figure 2391.

15       Figure 2393 shows a nucleotide sequence (SEQ ID NO:2393) of a native sequence PRO58796 cDNA, wherein SEQ ID NO:2393 is a clone designated herein as "DNA270415".

Figure 2394 shows the amino acid sequence (SEQ ID NO:2394) derived from the coding sequence of SEQ ID NO:2393 shown in Figure 2393.

20       Figure 2395 shows a nucleotide sequence (SEQ ID NO:2395) of a native sequence PRO84172 cDNA, wherein SEQ ID NO:2395 is a clone designated herein as "DNA328302".

Figure 2396 shows the amino acid sequence (SEQ ID NO:2396) derived from the coding sequence of SEQ ID NO:2395 shown in Figure 2395.

Figure 2397 shows a nucleotide sequence (SEQ ID NO:2397) of a native sequence PRO69467 cDNA, wherein SEQ ID NO:2397 is a clone designated herein as "DNA287178".

25       Figure 2398 shows the amino acid sequence (SEQ ID NO:2398) derived from the coding sequence of SEQ ID NO:2397 shown in Figure 2397.

Figure 2399 shows a nucleotide sequence (SEQ ID NO:2399) of a native sequence PRO84173 cDNA, wherein SEQ ID NO:2399 is a clone designated herein as "DNA328303".

30       Figure 2400 shows the amino acid sequence (SEQ ID NO:2400) derived from the coding sequence of SEQ ID NO:2399 shown in Figure 2399.

Figure 2401 shows a nucleotide sequence (SEQ ID NO:2401) of a native sequence PRO81319 cDNA, wherein SEQ ID NO:2401 is a clone designated herein as "DNA324684".

Figure 2402 shows the amino acid sequence (SEQ ID NO:2402) derived from the coding sequence of SEQ ID NO:2401 shown in Figure 2401.

35       Figure 2403 shows a nucleotide sequence (SEQ ID NO:2403) of a native sequence PRO84174 cDNA, wherein SEQ ID NO:2403 is a clone designated herein as "DNA328304".

Figure 2404 shows the amino acid sequence (SEQ ID NO:2404) derived from the coding sequence of SEQ ID NO:2403 shown in Figure 2403.

40       Figure 2405A-B shows a nucleotide sequence (SEQ ID NO:2405) of a native sequence cDNA, wherein SEQ ID NO:2405 is a clone designated herein as "DNA256131".

Figure 2406 shows a nucleotide sequence (SEQ ID NO:2406) of a native sequence PRO90 cDNA, wherein SEQ ID NO:2406 is a clone designated herein as "DNA328305".

Figure 2407 shows the amino acid sequence (SEQ ID NO:2407) derived from the coding sequence of SEQ ID NO:2406 shown in Figure 2406.

5        Figure 2408 shows a nucleotide sequence (SEQ ID NO:2408) of a native sequence PRO84175 cDNA, wherein SEQ ID NO:2408 is a clone designated herein as "DNA328306".

Figure 2409 shows the amino acid sequence (SEQ ID NO:2409) derived from the coding sequence of SEQ ID NO:2408 shown in Figure 2408.

10       Figure 2410A-B shows a nucleotide sequence (SEQ ID NO:2410) of a native sequence cDNA, wherein SEQ ID NO:2410 is a clone designated herein as "DNA255654".

Figure 2411 shows a nucleotide sequence (SEQ ID NO:2411) of a native sequence PRO84176 cDNA, wherein SEQ ID NO:2411 is a clone designated herein as "DNA328307".

Figure 2412 shows the amino acid sequence (SEQ ID NO:2412) derived from the coding sequence of SEQ ID NO:2411 shown in Figure 2411.

15       Figure 2413 shows a nucleotide sequence (SEQ ID NO:2413) of a native sequence cDNA, wherein SEQ ID NO:2413 is a clone designated herein as "DNA254447".

Figure 2414 shows a nucleotide sequence (SEQ ID NO:2414) of a native sequence PRO84177 cDNA, wherein SEQ ID NO:2414 is a clone designated herein as "DNA328308".

20       Figure 2415 shows the amino acid sequence (SEQ ID NO:2415) derived from the coding sequence of SEQ ID NO:2415 shown in Figure .

Figure 2416 shows a nucleotide sequence (SEQ ID NO:2416) of a native sequence cDNA, wherein ~~SEQ ID NO:2416 is a clone designated herein as "DNA256422".~~

Figure 2417 shows a nucleotide sequence (SEQ ID NO:2417) of a native sequence cDNA, wherein SEQ ID NO:2417 is a clone designated herein as "DNA255754".

25       Figure 2418 shows a nucleotide sequence (SEQ ID NO:2418) of a native sequence PRO50081 cDNA, wherein SEQ ID NO:2418 is a clone designated herein as "DNA328309".

Figure 2419 shows the amino acid sequence (SEQ ID NO:2419) derived from the coding sequence of SEQ ID NO:2418 shown in Figure 2418.

30       Figure 2420 shows a nucleotide sequence (SEQ ID NO:2420) of a native sequence cDNA, wherein SEQ ID NO:2420 is a clone designated herein as "DNA254286".

Figure 2421 shows a nucleotide sequence (SEQ ID NO:2421) of a native sequence cDNA, wherein SEQ ID NO:2421 is a clone designated herein as "DNA328310".

Figure 2422 shows a nucleotide sequence (SEQ ID NO:2422) of a native sequence PRO84179 cDNA, wherein SEQ ID NO:2422 is a clone designated herein as "DNA328311".

35       Figure 2423 shows the amino acid sequence (SEQ ID NO:2423) derived from the coding sequence of SEQ ID NO:2422 shown in Figure 2422.

Figure 2424 shows a nucleotide sequence (SEQ ID NO:2424) of a native sequence PRO82369 cDNA, wherein SEQ ID NO:2424 is a clone designated herein as "DNA325915".

40       Figure 2425 shows the amino acid sequence (SEQ ID NO:2425) derived from the coding sequence of SEQ ID NO:2424 shown in Figure 2424.

Figure 2426A-B shows a nucleotide sequence (SEQ ID NO:2426) of a native sequence PRO58642 cDNA, wherein SEQ ID NO:2426 is a clone designated herein as "DNA270254".

Figure 2427 shows the amino acid sequence (SEQ ID NO:2427) derived from the coding sequence of SEQ ID NO:2426 shown in Figure 2426A-B.

5        Figure 2428 shows a nucleotide sequence (SEQ ID NO:2428) of a native sequence PRO63223 cDNA, wherein SEQ ID NO:2428 is a clone designated herein as "DNA275594".

Figure 2429 shows the amino acid sequence (SEQ ID NO:2429) derived from the coding sequence of SEQ ID NO:2428 shown in Figure 2428.

10       Figure 2430 shows a nucleotide sequence (SEQ ID NO:2430) of a native sequence PRO50363 cDNA, wherein SEQ ID NO:2430 is a clone designated herein as "DNA255289".

Figure 2431 shows the amino acid sequence (SEQ ID NO:2431) derived from the coding sequence of SEQ ID NO:2430 shown in Figure 2430.

Figure 2432A-B shows a nucleotide sequence (SEQ ID NO:2432) of a native sequence PRO84180 cDNA, wherein SEQ ID NO:2432 is a clone designated herein as "DNA328312".

15       Figure 2433 shows the amino acid sequence (SEQ ID NO:2433) derived from the coding sequence of SEQ ID NO:2432 shown in Figure 2432.

Figure 2434 shows a nucleotide sequence (SEQ ID NO:2434) of a native sequence PRO82174 cDNA, wherein SEQ ID NO:2434 is a clone designated herein as "DNA325685".

20       Figure 2435 shows the amino acid sequence (SEQ ID NO:2435) derived from the coding sequence of SEQ ID NO:2434 shown in Figure 2434.

Figure 2436 shows a nucleotide sequence (SEQ ID NO:2436) of a native sequence PRO50218 cDNA, wherein SEQ ID NO:2436 is a clone designated herein as "DNA255137".

Figure 2437 shows the amino acid sequence (SEQ ID NO:2437) derived from the coding sequence of SEQ ID NO:2436 shown in Figure 2436.

25       Figure 2438 shows a nucleotide sequence (SEQ ID NO:2438) of a native sequence PRO84181 cDNA, wherein SEQ ID NO:2438 is a clone designated herein as "DNA328313".

Figure 2439 shows the amino acid sequence (SEQ ID NO:2439) derived from the coding sequence of SEQ ID NO:2438 shown in Figure 2438.

30       Figure 2440 shows a nucleotide sequence (SEQ ID NO:2440) of a native sequence PRO84182 cDNA, wherein SEQ ID NO:2440 is a clone designated herein as "DNA328314".

Figure 2441 shows the amino acid sequence (SEQ ID NO:2441) derived from the coding sequence of SEQ ID NO:2440 shown in Figure 2440.

Figure 2442 shows a nucleotide sequence (SEQ ID NO:2442) of a native sequence PRO84183 cDNA, wherein SEQ ID NO:2442 is a clone designated herein as "DNA328315".

35       Figure 2443 shows the amino acid sequence (SEQ ID NO:2443) derived from the coding sequence of SEQ ID NO:2442 shown in Figure 2442.

Figure 2444 shows a nucleotide sequence (SEQ ID NO:2444) of a native sequence PRO50231 cDNA, wherein SEQ ID NO:2444 is a clone designated herein as "DNA255151".

40       Figure 2445 shows the amino acid sequence (SEQ ID NO:2445) derived from the coding sequence of SEQ ID NO:2444 shown in Figure 2444.



Figure 2446 shows a nucleotide sequence (SEQ ID NO:2446) of a native sequence cDNA, wherein SEQ ID NO:2446 is a clone designated herein as "DNA256055".

Figure 2447 shows a nucleotide sequence (SEQ ID NO:2447) of a native sequence PRO84184 cDNA, wherein SEQ ID NO:2447 is a clone designated herein as "DNA328316".

5 Figure 2448 shows the amino acid sequence (SEQ ID NO:2448) derived from the coding sequence of SEQ ID NO:2447 shown in Figure 2447.

Figure 2449 shows a nucleotide sequence (SEQ ID NO:2449) of a native sequence PRO69493 cDNA, wherein SEQ ID NO:2449 is a clone designated herein as "DNA328317".

10 Figure 2450 shows the amino acid sequence (SEQ ID NO:2450) derived from the coding sequence of SEQ ID NO:2449 shown in Figure 2449.

Figure 2451 shows a nucleotide sequence (SEQ ID NO:2451) of a native sequence PRO84185 cDNA, wherein SEQ ID NO:2451 is a clone designated herein as "DNA328318".

Figure 2452 shows the amino acid sequence (SEQ ID NO:2452) derived from the coding sequence of SEQ ID NO:2451 shown in Figure 2451.

15 Figure 2453 shows a nucleotide sequence (SEQ ID NO:2453) of a native sequence PRO38240 cDNA, wherein SEQ ID NO:2453 is a clone designated herein as "DNA227777".

Figure 2454 shows the amino acid sequence (SEQ ID NO:2454) derived from the coding sequence of SEQ ID NO:2453 shown in Figure 2453.

20 Figure 2455 shows a nucleotide sequence (SEQ ID NO:2455) of a native sequence cDNA, wherein SEQ ID NO:2455 is a clone designated herein as "DNA328319".

Figure 2456A-B shows a nucleotide sequence (SEQ ID NO:2456) of a native sequence PRO84187 cDNA, wherein SEQ ID NO:2456 is a clone designated herein as "DNA328320".

Figure 2457 shows the amino acid sequence (SEQ ID NO:2457) derived from the coding sequence of SEQ ID NO:2457 shown in Figure .

25 Figure 2458 shows a nucleotide sequence (SEQ ID NO:2458) of a native sequence PRO84188 cDNA, wherein SEQ ID NO: 2458 is a clone designated herein as "DNA328321".

Figure 2459 shows the amino acid sequence (SEQ ID NO:2459) derived from the coding sequence of SEQ ID NO:2458 shown in Figure 2458.

30 Figure 2460 shows a nucleotide sequence (SEQ ID NO:2460) of a native sequence PRO54445 cDNA, wherein SEQ ID NO:2460 is a clone designated herein as "DNA260519".

Figure 2461 shows the amino acid sequence (SEQ ID NO:2461) derived from the coding sequence of SEQ ID NO:2460 shown in Figure 2460.

Figure 2462 shows a nucleotide sequence (SEQ ID NO:2462) of a native sequence cDNA, wherein SEQ ID NO:2462 is a clone designated herein as "DNA328322".

35 Figure 2463 shows a nucleotide sequence (SEQ ID NO:2463) of a native sequence cDNA, wherein SEQ ID NO:2463 is a clone designated herein as "DNA257960".

Figure 2464 shows a nucleotide sequence (SEQ ID NO:2464) of a native sequence PRO69531 cDNA, wherein SEQ ID NO:2464 is a clone designated herein as "DNA328323".

40 Figure 2465 shows the amino acid sequence (SEQ ID NO:2465) derived from the coding sequence of SEQ ID NO:2464 shown in Figure 2464.

Figure 2466 shows a nucleotide sequence (SEQ ID NO:2466) of a native sequence cDNA, wherein SEQ ID NO:2466 is a clone designated herein as "DNA262448".

Figure 2467 shows a nucleotide sequence (SEQ ID NO:2467) of a native sequence PRO84189 cDNA, wherein SEQ ID NO:2467 is a clone designated herein as "DNA328324".

5        Figure 2468 shows the amino acid sequence (SEQ ID NO:2468) derived from the coding sequence of SEQ ID NO:2467 shown in Figure 2467.

Figure 2469 shows a nucleotide sequence (SEQ ID NO:2469) of a native sequence cDNA, wherein SEQ ID NO:2469 is a clone designated herein as "DNA259231".

10       Figure 2470 shows a nucleotide sequence (SEQ ID NO:2470) of a native sequence cDNA, wherein SEQ ID NO:2470 is a clone designated herein as "DNA259493".

Figure 2471A-B shows a nucleotide sequence (SEQ ID NO:2471) of a native sequence PRO84190 cDNA, wherein SEQ ID NO:2471 is a clone designated herein as "DNA328325".

Figure 2472 shows the amino acid sequence (SEQ ID NO:2472) derived from the coding sequence of SEQ ID NO:2471 shown in Figure 2471.

15       Figure 2473 shows a nucleotide sequence (SEQ ID NO:2473) of a native sequence PRO84191 cDNA, wherein SEQ ID NO:2473 is a clone designated herein as "DNA328326".

Figure 2474 shows the amino acid sequence (SEQ ID NO:2474) derived from the coding sequence of SEQ ID NO:2473 shown in Figure 2473.

20       Figure 2475 shows a nucleotide sequence (SEQ ID NO:2475) of a native sequence cDNA, wherein SEQ ID NO:2475 is a clone designated herein as "DNA260507".

Figure 2476 shows a nucleotide sequence (SEQ ID NO:2476) of a native sequence cDNA, wherein ~~SEQ ID NO:2476 is a clone designated herein as "DNA262598".~~

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Figure 2477 shows a nucleotide sequence (SEQ ID NO:2477) of a native sequence cDNA, wherein SEQ ID NO:2477 is a clone designated herein as "DNA259663".

25       Figure 2478 shows a nucleotide sequence (SEQ ID NO:2478) of a native sequence cDNA, wherein SEQ ID NO:2478 is a clone designated herein as "DNA260543".

Figure 2479 shows a nucleotide sequence (SEQ ID NO:2479) of a native sequence cDNA, wherein SEQ ID NO:2479 is a clone designated herein as "DNA262755".

30       Figure 2480 shows a nucleotide sequence (SEQ ID NO:2480) of a native sequence cDNA, wherein SEQ ID NO:2480 is a clone designated herein as "DNA262761".

Figure 2481 shows a nucleotide sequence (SEQ ID NO:2481) of a native sequence PRO84192 cDNA, wherein SEQ ID NO:2481 is a clone designated herein as "DNA328327".

Figure 2482 shows the amino acid sequence (SEQ ID NO:2482) derived from the coding sequence of SEQ ID NO:2481 shown in Figure 2481.

35       Figure 2483 shows a nucleotide sequence (SEQ ID NO:2483) of a native sequence PRO84193 cDNA, wherein SEQ ID NO:2483 is a clone designated herein as "DNA328328".

Figure 2484 shows the amino acid sequence (SEQ ID NO:2484) derived from the coding sequence of SEQ ID NO:2483 shown in Figure 2483.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTSI. Definitions

The terms "PRO polypeptide" and "PRO" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and "PRO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods. The term "PRO polypeptide" refers to each individual PRO/number polypeptide disclosed herein. All disclosures in this specification which refer to the "PRO polypeptide" refer to each of the polypeptides individually as well as jointly. For example, descriptions of the preparation of, purification of, derivation of, formation of antibodies to or against, administration of, compositions containing, treatment of a disease with, etc., pertain to each polypeptide of the invention individually. The term "PRO polypeptide" also includes variants of the PRO/number polypeptides disclosed herein.

A "native sequence PRO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (*e.g.*, an extracellular domain sequence), naturally-occurring variant forms (*e.g.*, alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the invention, the native sequence PRO polypeptides disclosed herein are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in bold font and underlined in the figures.

However, while the PRO polypeptide disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the present specification and/or the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (e.g., Nielsen et al., Prot. Eng. 10:1-6 (1997) and von Heinje et al., Nucl. Acids. Res. 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a secreted polypeptide is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present invention.

"PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, ~~alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, alternatively at least about 20 amino acids in length, alternatively at least about 30 amino acids in length, alternatively at least about 40 amino acids in length, alternatively at least about 50 amino acids in length, alternatively at least about 60 amino acids in length, alternatively at least about 70 amino acids in length, alternatively at least about 80 amino acids in length, alternatively at least about 90 amino acids in length, alternatively at least about 100 amino acids in length,~~

alternatively at least about 150 amino acids in length, alternatively at least about 200 amino acids in length, alternatively at least about 300 amino acids in length, or more.

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this method, Tables 2 and 3 demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated "Comparison Protein" to the amino acid sequence designated "PRO", wherein "PRO" represents the amino acid sequence of a hypothetical PRO polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide against which the "PRO" polypeptide of interest is being compared, and "X," "Y" and "Z" each represent different hypothetical amino acid residues.

Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

However, % amino acid sequence identity values may also be obtained as described below by using the WU-

BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native PRO polypeptide and the comparison amino acid sequence of interest (i.e., the sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of interest.

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

where X is the number of amino acid residues scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

"PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid

sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity with a nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 210 nucleotides in length, alternatively at least about 240 nucleotides in length, alternatively at least about 270 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 900 nucleotides in length, or more.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence

D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

$$100 \text{ times the fraction } W/Z$$

5

where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA", wherein "PRO-DNA" represents a hypothetical PRO-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides.

Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % nucleic acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid sequence identity to the nucleic acid sequence B", the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest.

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acids Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.



In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

5

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C.

In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide *in situ* within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated" PRO polypeptide-encoding nucleic acid or other polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the polypeptide-encoding nucleic acid. An isolated polypeptide-encoding nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated polypeptide-encoding nucleic acid molecules therefore are distinguished from the specific polypeptide-encoding nucleic acid molecule as it exists in natural cells. However, an isolated polypeptide-encoding nucleic acid molecule includes polypeptide-encoding nucleic acid molecules contained in cells that ordinarily express the polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a

solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO polypeptide fused to a "tag polypeptide". The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

~~"Active" or "activity" for the purposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein "biological" activity refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO and an "immunological" activity refers to the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO.~~

The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics a biological activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the PRO polypeptide.

"Treatment" refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those

in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time.

5 "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

"Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

10 Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of  
15 physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating  
20 agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG), and PLURONIC™.

~~"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen-binding or~~  
variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')<sub>2</sub>, and Fv  
fragments; diabodies; linear antibodies (Zapata et al., Protein Eng. 8(10): 1057-1062 [1995]); single-chain  
25 antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an F(ab')<sub>2</sub> fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

30 "Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the V<sub>H</sub>-V<sub>L</sub> dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising  
35 only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge  
40 region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains

bear a free thiol group. F(ab')<sub>2</sub> antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their

5 constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2.

10 "Single-chain Fv" or "sFv" antibody fragments comprise the V<sub>H</sub> and V<sub>L</sub> domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the V<sub>H</sub> and V<sub>L</sub> domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

15 The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (V<sub>H</sub>) connected to a light-chain variable domain (V<sub>L</sub>) in the same polypeptide chain (V<sub>H</sub>-V<sub>L</sub>). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO  
20 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. ~~Contaminant components of its natural environment are materials~~ which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody  
25 will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the  
30 antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

An antibody that "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide is one that binds to that particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope.

35 The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can  
40 adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass

(e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No.

5 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

10 A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

The term "immune related disease" means a disease in which a component of the immune system of a mammal causes, mediates or otherwise contributes to a morbidity in the mammal. Also included are diseases in which stimulation or intervention of the immune response has an ameliorative effect on progression of the disease. Included within this term are immune-mediated inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency diseases, neoplasia, *etc.*

15 The term "T cell mediated disease" means a disease in which T cells directly or indirectly mediate or otherwise contribute to a morbidity in a mammal. The T cell mediated disease may be associated with cell mediated effects, lymphokine mediated effects, *etc.*, and even effects associated with B cells if the B cells are stimulated, for example, by the lymphokines secreted by T cells.

20 As used herein the term "psoriasis" is defined as a condition characterized by the eruption of circumscribed, discreet and confluent, reddish, silvery-scaled macropapules preeminently on the elbows, knees, scalp or trunk.

The term "effective amount" is a concentration or amount of a PRO polypeptide and/or agonist/antagonist which results in achieving a particular stated purpose. An "effective amount" of a PRO polypeptide or agonist or antagonist thereof may be determined empirically. Furthermore, a "therapeutically effective amount" is a concentration or amount of a PRO polypeptide and/or agonist/antagonist which is effective for achieving a stated therapeutic effect. This amount may also be determined empirically.

25 The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (e.g.,  $I^{131}$ ,  $I^{125}$ ,  $Y^{90}$  and  $Re^{186}$ ), chemotherapeutic agents, and toxins such as enzymatically active toxins of bacterial, fungal, plant or animal origin, or fragments thereof.

30 A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include adriamycin, doxorubicin, epirubicin, 5-fluorouracil, cytosine arabinoside ("Ara-C"), cyclophosphamide, thiotepa, busulfan, cytoxin, taxoids, e.g., paclitaxel (Taxol, Bristol-Myers Squibb Oncology, Princeton, NJ), and doxetaxel (Taxotere, Rhône-Poulenc Rorer, Antony, France), toxotere, methotrexate, cisplatin, melphalan, vinblastine, bleomycin, etoposide, ifosfamide, mitomycin C, mitoxantrone, vincristine, vinorelbine, carboplatin, teniposide, daunomycin, carminomycin, aminopterin, dactinomycin, mitomycins, esperamicins (see U.S. Pat. No. 4,675,187), melphalan and other related nitrogen mustards. Also included in this definition are hormonal agents that act to regulate or inhibit hormone action on tumors such as tamoxifen and onapristone.

40

A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell, especially cancer cell overexpressing any of the genes identified herein, either *in vitro* or *in vivo*. Thus, the growth inhibitory agent is one which significantly reduces the percentage of cells overexpressing such genes in S phase. Examples of growth inhibitory agents include agents that block cell cycle progression (at a place other than S phase), such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vincas (vincristine and vinblastine), taxol, and topo II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in *The Molecular Basis of Cancer*, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogens, and antineoplastic drugs" by Murakami *et al.* (WB Saunders: Philadelphia, 1995), especially p. 13.

The term "cytokine" is a generic term for proteins released by one cell population which act on another cell as intercellular mediators. Examples of such cytokines are lymphokines, monokines, and traditional polypeptide hormones. Included among the cytokines are growth hormone such as human growth hormone, N-methionyl human growth hormone, and bovine growth hormone; parathyroid hormone; thyroxine; insulin; proinsulin; relaxin; prorelaxin; glycoprotein hormones such as follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and luteinizing hormone (LH); hepatic growth factor; fibroblast growth factor; prolactin; placental lactogen; tumor necrosis factor- $\alpha$  and - $\beta$ ; mullerian-inhibiting substance; mouse gonadotropin-associated peptide; inhibin; activin; vascular endothelial growth factor; integrin; thrombopoietin (TPO); nerve growth factors such as NGF- $\beta$ ; platelet-growth factor; transforming growth factors (TGFs) such as TGF- $\alpha$  and TGF- $\beta$ ; insulin-like growth factor-I and -II; erythropoietin (EPO); osteoinductive factors; interferons such as interferon- $\alpha$ , - $\beta$ , and - $\gamma$ ; colony stimulating factors (CSFs) such as macrophage-CSF (M-CSF); granulocyte-macrophage-CSF (GM-CSF); and granulocyte-CSF (G-CSF); interleukins (ILs) such as IL-1, IL-1 $\alpha$ , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12; a tumor necrosis factor such as TNF- $\alpha$  or TNF- $\beta$ ; and other polypeptide factors including LIF and kit ligand (KL). As used herein, the term cytokine includes proteins from natural sources or from recombinant cell culture and biologically active equivalents of the native sequence cytokines.

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (*i.e.*, is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

As used herein, the term "inflammatory cells" designates cells that enhance the inflammatory response such as mononuclear cells, eosinophils, macrophages, and polymorphonuclear neutrophils (PMN).

Table 1

```

/*
5  *
  * C-C increased from 12 to 15
  * Z is average of EQ
  * B is average of ND
  * match with stop is _M; stop-stop = 0; J (joker) match = 0
10 */
#define _M      -8      /* value of a match with a stop */

int      _day[26][26] = {
/*      A B C D E F G H I J K L M N O P Q R S T U V W X Y Z */
15 /* A */      { 2, 0, -2, 0, 0, -4, 1, -1, -1, 0, -1, -2, -1, 0, _M, 1, 0, -2, 1, 1, 0, 0, -6, 0, -3, 0},
/* B */      { 0, 3, -4, 3, 2, -5, 0, 1, -2, 0, 0, -3, -2, 2, _M, -1, 1, 0, 0, 0, 0, -2, -5, 0, -3, 1},
/* C */      {-2, -4, 15, -5, -5, -4, -3, -2, 0, -5, -6, -5, -4, _M, -3, -5, -4, 0, -2, 0, -2, -8, 0, 0, -5},
/* D */      { 0, 3, -5, 4, 3, -6, 1, 1, -2, 0, 0, -4, -3, 2, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 2},
/* E */      { 0, 2, -5, 3, 4, -5, 0, 1, -2, 0, 0, -3, -2, 1, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 3},
20 /* F */      {-4, -5, -4, -6, -5, 9, -5, -2, 1, 0, -5, 2, 0, -4, _M, -5, -5, -4, -3, -3, 0, -1, 0, 0, 7, -5},
/* G */      { 1, 0, -3, 1, 0, -5, 5, -2, -3, 0, -2, -4, -3, 0, _M, -1, -1, -3, 1, 0, 0, -1, -7, 0, -5, 0},
/* H */      {-1, 1, -3, 1, 1, -2, -2, 6, -2, 0, 0, -2, -2, 2, _M, 0, 3, 2, -1, -1, 0, -2, -3, 0, 0, 2},
/* I */      {-1, -2, -2, -2, -2, 1, -3, -2, 5, 0, -2, 2, 2, -2, _M, -2, -2, -2, -1, 0, 0, 4, -5, 0, -1, -2},
/* J */      { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0},
25 /* K */      {-1, 0, -5, 0, 0, -5, -2, 0, -2, 0, 5, -3, 0, 1, _M, -1, 1, 3, 0, 0, 0, -2, -3, 0, -4, 0},
/* L */      {-2, -3, -6, -4, -3, 2, -4, -2, 2, 0, -3, 6, 4, -3, _M, -3, -2, -3, -3, -1, 0, 2, -2, 0, -1, -2},
/* M */      {-1, -2, -5, -3, -2, 0, -3, -2, 2, 0, 0, 4, 6, -2, _M, -2, -1, 0, -2, -1, 0, 2, -4, 0, -2, -1},
/* N */      { 0, 2, -4, 2, 1, -4, 0, 2, -2, 0, 1, -3, -2, 2, _M, -1, 1, 0, 1, 0, 0, -2, -4, 0, -2, 1},
/* O */      {_M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, 0, _M, _M, _M, _M, _M, _M, _M, _M, _M},
30 /* P */      { 1, -1, -3, -1, -1, -5, -1, 0, -2, 0, -1, -3, -2, -1, _M, 6, 0, 0, 1, 0, 0, -1, -6, 0, -5, 0},
/* Q */      { 0, 1, -5, 2, 2, -5, -1, 3, -2, 0, 1, -2, -1, 1, _M, 0, 4, 1, -1, -1, 0, -2, -5, 0, -4, 3},
/* R */      {-2, 0, -4, -1, -1, -4, -3, 2, -2, 0, 3, -3, 0, 0, _M, 0, 1, 6, 0, -1, 0, -2, 2, 0, -4, 0},
/* S */      { 1, 0, 0, 0, 0, -3, 1, -1, -1, 0, 0, -3, -2, 1, _M, 1, -1, 0, 2, 1, 0, -1, -2, 0, -3, 0},
/* T */      { 1, 0, -2, 0, 0, -3, 0, -1, 0, 0, 0, -1, -1, 0, _M, 0, -1, -1, 1, 3, 0, 0, -5, 0, -3, 0},
35 /* U */      { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* V */      { 0, -2, -2, -2, -2, -1, -1, -2, 4, 0, -2, 2, 2, -2, _M, -1, -2, -2, -1, 0, 0, 4, -6, 0, -2, -2},
/* W */      {-6, -5, -8, -7, -7, 0, -7, -3, -5, 0, -3, -2, -4, -4, _M, -6, -5, 2, -2, -5, 0, -6, 17, 0, 0, -6},
/* X */      { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* Y */      {-3, -3, 0, -4, -4, 7, -5, 0, -1, 0, -4, -1, -2, -2, _M, -5, -4, -4, -3, -3, 0, -2, 0, 0, 10, -4},
40 /* Z */      { 0, 1, -5, 2, 3, -5, 0, 2, -2, 0, 0, -2, -1, 1, _M, 0, 3, 0, 0, 0, 0, -2, -6, 0, -4, 4}
};

```



**Table 1 (cont')**

```

/*
*/
#include <stdio.h>
#include <ctype.h>

#define MAXJMP      16      /* max jumps in a diag */
#define MAXGAP      24      /* don't continue to penalize gaps larger than this */
#define JMPS        1024    /* max jmps in an path */
10  #define MX         4      /* save if there's at least MX-1 bases since last jmp */

#define DMAT         3      /* value of matching bases */
#define DMIS         0      /* penalty for mismatched bases */
#define DINSO        8      /* penalty for a gap */
15  #define DINS1      1      /* penalty per base */
#define PINSO        8      /* penalty for a gap */
#define PINS1        4      /* penalty per residue */

struct jmp {
20     short          n[MAXJMP];    /* size of jmp (neg for dely) */
     unsigned short x[MAXJMP];    /* base no. of jmp in seq x */
};                                /* limits seq to 2^16 -1 */

struct diag {
25     int            score;        /* score at last jmp */
     long           offset;       /* offset of prev block */
     short          jmp;         /* current jmp index */
     struct jmp     jp;          /* list of jmps */
};

30  struct path {
     int            spc;          /* number of leading spaces */
     short          n[JMPS];     /* size of jmp (gap) */
     int            x[JMPS];     /* loc of jmp (last elem before gap) */
35  };

char      *ofile;                /* output file name */
char      *namex[2];             /* seq names: getseqs() */
40  char      *prog;              /* prog name for err msgs */
char      *seqx[2];             /* seqs: getseqs() */
int        dmax;                /* best diag: nw() */
int        dmax0;               /* final diag */
int        dna;                 /* set if dna: main() */
int        endgaps;             /* set if penalizing end gaps */
45  int        gapx, gapy;        /* total gaps in seqs */
int        len0, len1;          /* seq lens */
int        ngapx, ngapy;        /* total size of gaps */
int        smax;                /* max score: nw() */
int        *xbm;                /* bitmap for matching */
50  long      offset;             /* current offset in jmp file */
struct     diag                /* holds diagonals */
struct     path                /* holds path for seqs */
        pp[2];

char      *calloc(), *malloc(), *index(), *strcpy();
55  char      *getseq(), *g_calloc();

```

60

**Table 1 (cont')**

```

/* Needleman-Wunsch alignment program
*
* usage: prog file1 file2
5  * where file1 and file2 are two dna or two protein sequences.
* The sequences can be in upper- or lower-case and may contain ambiguity
* Any lines beginning with ';', '>' or '<' are ignored
* Max file length is 65535 (limited by unsigned short x in the jmp struct)
* A sequence with 1/3 or more of its elements ACGTU is assumed to be DNA
10 * Output is in the file "align.out"
*
* The program may create a tmp file in /tmp to hold info about traceback.
* Original version developed under BSD 4.3 on a vax 8650
*/
15 #include "nw.h"
#include "day.h"

static _dbval[26] = {
20 1,14,2,13,0,0,4,11,0,0,12,0,3,15,0,0,0,5,6,8,8,7,9,0,10,0
};

static _pbval[26] = {
25 1, 2|(1<<('D'-'A'))|(1<<('N'-'A')), 4, 8, 16, 32, 64,
128, 256, 0xFFFFFFFF, 1<<10, 1<<11, 1<<12, 1<<13, 1<<14,
1<<15, 1<<16, 1<<17, 1<<18, 1<<19, 1<<20, 1<<21, 1<<22,
1<<23, 1<<24, 1<<25|(1<<('B'-'A'))|(1<<('Q'-'A'))
};

main(ac, av)
30 main
int ac;
char *av[ ];
{
prog = av[0];
35 if (ac != 3) {
fprintf(stderr, "usage: %s file1 file2\n", prog);
fprintf(stderr, "where file1 and file2 are two dna or two protein sequences.\n");
fprintf(stderr, "The sequences can be in upper- or lower-case\n");
fprintf(stderr, "Any lines beginning with ';', '>' or '<' are ignored\n");
40 fprintf(stderr, "Output is in the file \"align.out\"\n");
exit(1);
}
namex[0] = av[1];
namex[1] = av[2];
45 seqx[0] = getseq(namex[0], &len0);
seqx[1] = getseq(namex[1], &len1);
xbm = (dna)? _dbval : _pbval;

endgaps = 0; /* 1 to penalize endgaps */
50 ofile = "align.out"; /* output file */

nw(); /* fill in the matrix, get the possible jumps */
readjumps(); /* get the actual jumps */
print(); /* print stats, alignment */
55 cleanup(); /* unlink any tmp files */
}
60

```

**Table 1 (cont')**

```

/* do the alignment, return best score: main()
 * dna: values in Fitch and Smith, PNAS, 80, 1382-1386, 1983
 * pro: PAM 250 values
5  * When scores are equal, we prefer mismatches to any gap, prefer
 * a new gap to extending an ongoing gap, and prefer a gap in seqx
 * to a gap in seq y.
 */
nw()
10  nw
{
    char      *px, *py;      /* seqs and ptrs */
    int        *ndely, *dely; /* keep track of dely */
    int        ndelx, delx;   /* keep track of delx */
15  int        *tmp;         /* for swapping row0, row1 */
    int        mis;          /* score for each type */
    int        ins0, ins1;    /* insertion penalties */
    register   id;           /* diagonal index */
    register   ij;           /* jmp index */
20  register   *col0, *col1;  /* score for curr, last row */
    register   xx, yy;       /* index into seqs */

    dx = (struct diag *)g_calloc("to get diags", len0+len1+1, sizeof(struct diag));

25  ndely = (int *)g_calloc("to get ndely", len1+1, sizeof(int));
    dely = (int *)g_calloc("to get dely", len1+1, sizeof(int));
    col0 = (int *)g_calloc("to get col0", len1+1, sizeof(int));
    col1 = (int *)g_calloc("to get col1", len1+1, sizeof(int));
    ins0 = (dna)? DINS0 : PINS0;
30  ins1 = (dna)? DINS1 : PINS1;

    smax = -10000;
    if (endgaps) {
        for (col0[0] = dely[0] = -ins0, yy = 1; yy <= len1; yy++) {
35  col0[yy] = dely[yy] = col0[yy-1] - ins1;
            ndely[yy] = yy;
        }
        col0[0] = 0;      /* Waterman Bull Math Biol 84 */
    }
    else
40  for (yy = 1; yy <= len1; yy++)
        dely[yy] = -ins0;

    /* fill in match matrix
    */
45  for (px = seqx[0], xx = 1; xx <= len0; px++, xx++) {
        /* initialize first entry in col
        */
        if (endgaps) {
50  if (xx == 1)
            col1[0] = delx = -(ins0+ins1);
            else
            col1[0] = delx = col0[0] - ins1;
            ndelx = xx;
55  }
        else {
            col1[0] = 0;
            delx = -ins0;
            ndelx = 0;
60  }
    }

```

**Table 1 (cont')**

...nw

```

5      for (py = seqx[1], yy = 1; yy <= len1; py++, yy++) {
        mis = col0[yy-1];
        if (dna)
            mis += (xbm[*px-'A']&xbm[*py-'A'])? DMAT : DMIS;
        else
            mis += _day[*px-'A'][*py-'A'];
10      /* update penalty for del in x seq;
        * favor new del over ongong del
        * ignore MAXGAP if weighting endgaps
        */
        if (endgaps || ndely[yy] < MAXGAP) {
15          if (col0[yy] - ins0 >= dely[yy]) {
              dely[yy] = col0[yy] - (ins0+ins1);
              ndely[yy] = 1;
          } else {
              dely[yy] = ins1;
              ndely[yy]++;
20          }
        } else {
            if (col0[yy] - (ins0+ins1) >= dely[yy]) {
25                dely[yy] = col0[yy] - (ins0+ins1);
                ndely[yy] = 1;
            } else
                ndely[yy]++;
        }
30      /* update penalty for del in y seq;
        * favor new del over ongong del
        */
        if (endgaps || ndelx < MAXGAP) {
35          if (col1[yy-1] - ins0 >= delx) {
              delx = col1[yy-1] - (ins0+ins1);
              ndelx = 1;
          } else {
              delx = ins1;
              ndelx++;
40          }
        } else {
            if (col1[yy-1] - (ins0+ins1) >= delx) {
                delx = col1[yy-1] - (ins0+ins1);
                ndelx = 1;
45            } else
                ndelx++;
        }
50      /* pick the maximum score; we're favoring
        * mis over any del and delx over dely
        */

```

55

60

Table 1 (cont')

...nw

```

id = xx - yy + len1 - 1;
if (mis >= delx && mis >= dely[yy])
    coll[yy] = mis;
else if (delx >= dely[yy]) {
    coll[yy] = delx;
    ij = dx[id].ijmp;
    if (dx[id].jp.n[0] && (!dna || (ndelx >= MAXJMP
10    && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
        dx[id].ijmp++;
        if (++ij >= MAXJMP) {
            writeimps(id);
            ij = dx[id].ijmp = 0;
15            dx[id].offset = offset;
            offset += sizeof(struct jmp) + sizeof(offset);
        }
        dx[id].jp.n[ij] = ndelx;
        dx[id].jp.x[ij] = xx;
        dx[id].score = delx;
    }
    else {
25        coll[yy] = dely[yy];
        ij = dx[id].ijmp;
        if (dx[id].jp.n[0] && (!dna || (ndely[yy] >= MAXJMP
            && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
            dx[id].ijmp++;
            if (++ij >= MAXJMP) {
30                writeimps(id);
                ij = dx[id].ijmp = 0;
                dx[id].offset = offset;
                offset += sizeof(struct jmp) + sizeof(offset);
            }
35        }
        dx[id].jp.n[ij] = -ndely[yy];
        dx[id].jp.x[ij] = xx;
        dx[id].score = dely[yy];
    }
    if (xx == len0 && yy < len1) {
        /* last col
        */
        if (endgaps)
            coll[yy] -= ins0+ins1*(len1-yy);
45        if (coll[yy] > smax) {
            smax = coll[yy];
            dmax = id;
        }
    }
}
if (endgaps && xx < len0)
    coll[yy-1] -= ins0+ins1*(len0-xx);
if (coll[yy-1] > smax) {
50    smax = coll[yy-1];
    dmax = id;
}
tmp = col0; col0 = coll; coll = tmp;
}
(void) free((char *)ndely);
(void) free((char *)dely);
(void) free((char *)col0);
60 (void) free((char *)coll);
    }

```

Table 1 (cont')

```

/*
 *
 * print() -- only routine visible outside this module
5  *
 * static:
 * getmat() -- trace back best path, count matches: print()
 * pr_align() -- print alignment of described in array p[ ]: print()
 * dumpblock() -- dump a block of lines with numbers, stars: pr_align()
10 * nums() -- put out a number line: dumpblock()
 * putline() -- put out a line (name, [num], seq, [num]): dumpblock()
 * stars() -- put a line of stars: dumpblock()
 * stripname() -- strip any path and prefix from a seqname
 */
15
#include "nw.h"

#define SPC      3
#define P_LINE   256    /* maximum output line */
20 #define P_SPC   3      /* space between name or num and seq */

extern  _day[26][26];
int     olen;           /* set output line length */
FILE    *fx;           /* output file */
25

print()
{
    print
    {
        int     lx, ly, firstgap, lastgap;    /* overlap */
30
        if ((fx = fopen(ofile, "w")) == 0) {
            fprintf(stderr, "%s: can't write %s\n", prog, ofile);
            cleanup(1);
        }
35
        fprintf(fx, "<first sequence: %s (length = %d)\n", namex[0], len0);
        fprintf(fx, "<second sequence: %s (length = %d)\n", namex[1], len1);
        olen = 60;
        lx = len0;
        ly = len1;
        firstgap = lastgap = 0;
40
        if (dmax < len1 - 1) {    /* leading gap in x */
            pp[0].spc = firstgap = len1 - dmax - 1;
            ly -= pp[0].spc;
        }
        else if (dmax > len1 - 1) {    /* leading gap in y */
45
            pp[1].spc = firstgap = dmax - (len1 - 1);
            lx -= pp[1].spc;
        }
        if (dmax0 < len0 - 1) {    /* trailing gap in x */
50
            lastgap = len0 - dmax0 - 1;
            lx -= lastgap;
        }
        else if (dmax0 > len0 - 1) {    /* trailing gap in y */
55
            lastgap = dmax0 - (len0 - 1);
            ly -= lastgap;
        }
        getmat(lx, ly, firstgap, lastgap);
        pr_align();
60
    }
}

```

Table 1 (cont')

```

/*
 * trace back the best path, count matches
 */
5 static
  getmat(lx, ly, firstgap, lastgap)                                getmat
      int    lx, ly;                      /* "core" (minus endgaps) */
      int    firstgap, lastgap;          /* leading trailing overlap */
{
10     int      nm, i0, i1, siz0, siz1;
      char      outx[32];
      double     pct;
      register   n0, n1;
      register char *p0, *p1;

15     /* get total matches, score
      */
      i0 = i1 = siz0 = siz1 = 0;
      p0 = seqx[0] + pp[1].spc;
20     p1 = seqx[1] + pp[0].spc;
      n0 = pp[1].spc + 1;
      n1 = pp[0].spc + 1;

      nm = 0;
25     while ( *p0 && *p1 ) {
          if (siz0) {
              p1++;
              n1++;
              siz0--;
30          }
          else if (siz1) {
              p0++;
              n0++;
              siz1--;
35          }
          else {
              if (xbm[*p0-'A'] & xbm[*p1-'A'])
                  nm++;
              if (n0++ == pp[0].x[i0])
                  siz0 = pp[0].n[i0++];
40              if (n1++ == pp[1].x[i1])
                  siz1 = pp[1].n[i1++];
              p0++;
              p1++;
45          }
      }

      /* pct homology:
      * if penalizing endgaps, base is the shorter seq
50     * else, knock off overhangs and take shorter core
      */
      if (endgaps)
          lx = (len0 < len1)? len0 : len1;
      else
55         lx = (lx < ly)? lx : ly;
      pct = 100:*(double)nm/(double)lx;
      fprintf(fx, "\n");
      fprintf(fx, "<%d match%s in an overlap of %d: %.2f percent similarity\n",
60         nm, (nm == 1)? "" : "es", lx, pct);

```

**Table 1 (cont')**

```

    fprintf(fx, "<gaps in first sequence: %d", gapx);
    if (gapx) {
5         (void) sprintf(outx, " (%d %s%s)",
            ngapx, (dna)? "base":"residue", (ngapx == 1)? "" : "s");
            fprintf(fx, "%s", outx);

    fprintf(fx, ", gaps in second sequence: %d", gapy);
10    if (gapy) {
        (void) sprintf(outx, " (%d %s%s)",
            ngapy, (dna)? "base":"residue", (ngapy == 1)? "" : "s");
            fprintf(fx, "%s", outx);
    }
15    if (dna)
        fprintf(fx,
            "\n<score: %d (match = %d, mismatch = %d, gap penalty = %d + %d per base)\n",
            smax, DMAT, DMIS, DINS0, DINS1);
    else
20        fprintf(fx,
            "\n<score: %d (Dayhoff PAM 250 matrix, gap penalty = %d + %d per residue)\n",
            smax, PINS0, PINS1);
    if (endgaps)
25        fprintf(fx,
            "<endgaps penalized. left endgap: %d %s%s, right endgap: %d %s%s\n",
            firstgap, (dna)? "base" : "residue", (firstgap == 1)? "" : "s",
            lastgap, (dna)? "base" : "residue", (lastgap == 1)? "" : "s");
    else
        fprintf(fx, "<endgaps not penalized\n");
30 }
    static nm; /* matches in core — for checking */
    static lmax; /* lengths of stripped file names */
    static ij[2]; /* jmp index for a path */
    static nc[2]; /* number at start of current line */
35    static ni[2]; /* current elem number — for gapping */

    static siz[2];
    static char *ps[2]; /* ptr to current element */
    static char *po[2]; /* ptr to next output char slot */
    static char out[2][P_LINE]; /* output line */
40    static char star[P_LINE]; /* set by stars() */

    /*
     * print alignment of described in struct path pp[ ]
     */
45    static
    pr_align()
    {
        int nn; /* char count */
        int more;
50        register i;

        for (i = 0, lmax = 0; i < 2; i++) {
            nn = stripname(namex[i]);
            if (nn > lmax)
55                lmax = nn;

            nc[i] = 1;
            ni[i] = 1;
            siz[i] = ij[i] = 0;
60            ps[i] = seqx[i];
            po[i] = out[i];
        }

```

...getmat

pr\_align



Table 1 (cont')

...pr\_align

```

5      for (nn = nm = 0, more = 1; more; ) {
        for (i = more = 0; i < 2; i++) {
            /*
            * do we have more of this sequence?
            */
            if (!*ps[i])
                continue;

10         more++;

            if (pp[i].spc) { /* leading space */
                *po[i]++ = ' ';
                pp[i].spc--;
15         }
            else if (siz[i]) { /* in a gap */
                *po[i]++ = '-';
                siz[i]--;
20         }
            else { /* we're putting a seq element
                */
                *po[i] = *ps[i];
                if (islower(*ps[i]))
                    *ps[i] = toupper(*ps[i]);
                po[i]++;
                ps[i]++;

30         /*
            * are we at next gap for this seq?
            */
            if (ni[i] == pp[i].x[ij[i]]) {
                /*
                * we need to merge all gaps
                * at this location
                */
                siz[i] = pp[i].n[ij[i]]++;
                while (ni[i] == pp[i].x[ij[i]])
                    siz[i] += pp[i].n[ij[i]]++;
40         }
                ni[i]++;
            }
        }
        if (++nn == olen || !more && nn) {
            dumpblock();
            for (i = 0; i < 2; i++)
                po[i] = out[i];
            nn = 0;
50     }
    }

    /*
    * dump a block of lines, including numbers, stars: pr_align()
55  */
    static
    dumpblock()
    {
        register i;
        for (i = 0; i < 2; i++)
            *po[i]-- = '\0';
60

```

Table 1 (cont')

...dumpblock

```

5      (void) putc('\n', fx);
      for (i = 0; i < 2; i++) {
          if (*out[i] && (*out[i] != '' || *(po[i]) != ')) {
              if (i == 0)
                  nums(i);
              if (i == 0 && *out[1])
10                 stars();
              putline(i);
              if (i == 0 && *out[1])
                  fprintf(fx, star);
              if (i == 1)
15                 nums(i);
          }
      }
  }

20  /*
   * put out a number line: dumpblock()
   */
   static
   nums(ix)
25  {
      int      ix;      /* index in out[ ] holding seq line */
      char      nline[P_LINE];
      register  i, j;
      register char *pn, *px, *py;
30
      for (pn = nline, i = 0; i < lmax+P_SPC; i++, pn++)
          *pn = '\0';
      for (i = nc[ix], py = out[ix]; *py; py++, pn++) {
          if (*py == '' || *py == '\0')
35             *pn = '\0';
          else {
              if (i%10 == 0 || (i == 1 && nc[ix] != 1)) {
                  j = (i < 0)? -i : i;
                  for (px = pn; j /= 10, px--)
40                     *px = j%10 + '0';
                  if (i < 0)
                      *px = '-';
              }
              else
45                 *pn = '\0';
              i++;
          }
      }
      *pn = '\0';
      nc[ix] = i;
      for (pn = nline; *pn; pn++)
          (void) putc(*pn, fx);
      (void) putc('\n', fx);
55  }

  /*
   * put out a line (name, [num], seq, [num]): dumpblock()
   */
   static
   putline(ix)
60  {
      int      ix;

```

nums

putline

Table 1 (cont')

...putline

```

5      int          i;
      register char *px;

      for (px = namex[ix], i = 0; *px && *px != '\0'; px++, i++)
          (void) putc(*px, fx);
10     for (; i < lmax+P_SPC; i++)
          (void) putc(' ', fx);

      /* these count from 1:
       * ni[ ] is current element (from 1)
       * nc[ ] is number at start of current line
15     */
      for (px = out[ix]; *px; px++)
          (void) putc(*px&0x7F, fx);
      (void) putc('\n', fx);
20   }

      /*
       * put a line of stars (seqs always in out[0], out[1]): dumpblock()
       */
25   static
      stars()
      {
          int          i;
          register char *p0, *p1, cx, *px;

          if (!*out[0] || (*out[0] == '\0' && *(p0[0]) == '\0') ||
              !*out[1] || (*out[1] == '\0' && *(p0[1]) == '\0'))
              return;
35     px = stars;
          for (i = lmax+P_SPC; i; i--)
              *px++ = '\0';

          for (p0 = out[0], p1 = out[1]; *p0 && *p1; p0++, p1++) {
40             if (isalpha(*p0) && isalpha(*p1)) {

                  if (xbm[*p0-'A'] && xbm[*p1-'A']) {
                      cx = '\0';
                      nm++;
45                 }
                  else if (ldna && _day[*p0-'A'][*p1-'A'] > 0)
                      cx = '\0';
                  else
                      cx = ' ';
50             }
            else
                cx = ' ';
            *px++ = cx;
55     }
      *px++ = '\n';
      *px = '\0';
}
60

```

**Table 1 (cont')**

```
/*
 * strip path or prefix from pn, return len: pr_align0
 */
5 static
  stripname(pn)
      stripname
      char *pn; /* file name (may be path) */
10 {
      register char *px, *py;

      py = 0;
      for (px = pn; *px; px++)
          if (*px == '/')
15             py = px + 1;

      if (py)
          (void) strcpy(pn, py);
      return(strlen(pn));
20 }
```

25

30

35

40

45

50

55

60

Table 1 (cont')

```

/*
 * cleanup() - cleanup any tmp file
 * getseq() - read in seq, set dna, len, maxlen
5  * g_malloc() - calloc() with error checkin
 * readjumps() - get the good jumps, from tmp file if necessary
 * writejumps() - write a filled array of jumps to a tmp file: nw()
 */
#include "nw.h"
10 #include <sys/file.h>

char    *jname = "/tmp/homgXXXXXX";      /* tmp file for jumps */
FILE    *fj;

15 int    cleanup();                      /* cleanup tmp file */
long    lseek();

/*
 * remove any tmp file if we blow
20 */
cleanup(i)
    int    i;
{
    if (fj)
25     (void) unlink(jname);
    exit(i);
}

/*
30 * read, return ptr to seq, set dna, len, maxlen
 * skip lines starting with ',', '<', or '>'
 * seq in upper or lower case
 */
char    *
35 getseq(file, len)
    char    *file;    /* file name */
    int     *len;     /* seq len */
{
    char    line[1024], *pseq;
    register char    *px, *py;
    int     natgc, tlen;
    FILE    *fp;

    if ((fp = fopen(file, "r")) == 0) {
45         fprintf(stderr, "%s: can't read %s\n", prog, file);
        exit(1);
    }
    tlen = natgc = 0;
    while (fgets(line, 1024, fp)) {
50         if (*line == ',' || *line == '<' || *line == '>')
            continue;
        for (px = line; *px != '\n'; px++)
            if (isupper(*px) || islower(*px))
                tlen++;
55     }
    if ((pseq = malloc((unsigned)(tlen+6))) == 0) {
        fprintf(stderr, "%s: malloc() failed to get %d bytes for %s\n", prog, tlen+6, file);
        exit(1);
    }
    pseq[0] = pseq[1] = pseq[2] = pseq[3] = '\0';
60

```

cleanup

getseq

Table 1 (cont')

...getseq

```

    py = pseq + 4;
    *len = tlen;
5    rewind(fp);

    while (fgets(line, 1024, fp)) {
        if (*line == ';' || *line == '<' || *line == '>')
            continue;
10        for (px = line; *px != '\n'; px++) {
            if (isupper(*px))
                *py++ = *px;
            else if (islower(*px))
                *py++ = toupper(*px);
15            if (index("ATGCU", *(py-1)))
                natgc++;
        }
        *py++ = '\0';
        *py = '\0';
        (void) fclose(fp);
        dna = natgc > (tlen/3);
        return(pseq+4);
    }
25
char *
g_alloc(msg, nx, sz)
char *msg;          /* program, calling routine */
int nx, sz;          /* number and size of elements */
30 {
    char *px, *calloc();

    if ((px = calloc((unsigned)nx, (unsigned)sz)) == 0) {
        if (*msg) {
35            fprintf(stderr, "%s: g_alloc() failed %s (n=%d, sz=%d)\n", prog, msg, nx, sz);
            exit(1);
        }
    }
    return(px);
40 }

/*
 * get final jmps from dx[ ] or tmp file, set pp[ ], reset dmax: main()
 */
45 readjmps()
{
    readjmps
    {
        int fd = -1;
        int siz, i0, i1;
50        register i, j, xx;

        if (fj) {
            (void) fclose(fj);
            if ((fd = open(jname, O_RDONLY, 0)) < 0) {
55                fprintf(stderr, "%s: can't open() %s\n", prog, jname);
                cleanup(1);
            }
        }
        for (i = i0 = i1 = 0, dmax0 = dmax, xx = len0; ; i++) {
60            while (1) {
                for (j = dx[dmax].ijmp; j >= 0 && dx[dmax].jp.x[j] >= xx; j--)
                    ;
            }
        }
    }
}

```

g\_alloc

**Table 1 (cont')****...readjumps**

```

5      if (j < 0 && dx[dmax].offset && fj) {
        (void) lseek(fd, dx[dmax].offset, 0);
        (void) read(fd, (char *)&dx[dmax].jp, sizeof(struct jmp));
        (void) read(fd, (char *)&dx[dmax].offset, sizeof(dx[dmax].offset));
        dx[dmax].ijmp = MAXJMP-1;
      }
10     else
        break;
    }
    if (i >= JMPS) {
        fprintf(stderr, "%s: too many gaps in alignment\n", prog);
        cleanup(1);
15    }
    if (j >= 0) {
        siz = dx[dmax].jp.n[j];
        xx = dx[dmax].jp.x[j];
        dmax += siz;
20     if (siz < 0) { /* gap in second seq */
        pp[1].n[i1] = -siz;
        xx += siz;
        /* id = xx - yy + len1 - 1
        */
25     pp[1].x[i1] = xx - dmax + len1 - 1;
        gapy++;
        ngapy -= siz;
        /* ignore MAXGAP when doing endgaps */
        siz = (-siz < MAXGAP || endgaps)? -siz : MAXGAP;
30     i1++;
    }
    else if (siz > 0) { /* gap in first seq */
        pp[0].n[i0] = siz;
        pp[0].x[i0] = xx;
35     gapx++;
        ngapx += siz;
        /* ignore MAXGAP when doing endgaps */
        siz = (siz < MAXGAP || endgaps)? siz : MAXGAP;
40     i0++;
    }
    else
        break;
}

45 /* reverse the order of jumps
*/
for (j = 0, i0--; j < i0; j++, i0--) {
    i = pp[0].n[j]; pp[0].n[j] = pp[0].n[i0]; pp[0].n[i0] = i;
50     i = pp[0].x[j]; pp[0].x[j] = pp[0].x[i0]; pp[0].x[i0] = i;
}
for (j = 0, i1--; j < i1; j++, i1--) {
    i = pp[1].n[j]; pp[1].n[j] = pp[1].n[i1]; pp[1].n[i1] = i;
55     i = pp[1].x[j]; pp[1].x[j] = pp[1].x[i1]; pp[1].x[i1] = i;
}
if (fd >= 0)
    (void) close(fd);
if (fj) {
60     (void) unlink(jname);
    fj = 0;
    offset = 0;
}
}

```

**Table 1 (cont')**

```

/*
5  * write a filled jmp struct offset of the prev one (if any): nw()
   */
   writejumps(ix)
       writejumps
           int    ix;
10  {
       char    *mktemp();

           if (!fj) {
               if (mktemp(jname) < 0) {
15                 fprintf(stderr, "%s: can't mktemp() %s\n", prog, jname);
                   cleanup(1);
               }
               if ((fj = fopen(jname, "w")) == 0) {
                   fprintf(stderr, "%s: can't write %s\n", prog, jname);
20                 exit(1);
               }
           }
       }
       (void) fwrite((char *)&dx[ix].jp, sizeof(struct jmp), 1, fj);
       (void) fwrite((char *)&dx[ix].offset, sizeof(dx[ix].offset), 1, fj);
25   }

```



Table 2

5 PRO XXXXXXXXXXXXXXXX (Length = 15 amino acids)  
 Comparison Protein XXXXXYYYYYYY (Length = 12 amino acids)  
 % amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as  
 10 determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =  
 5 divided by 15 = 33.3%

Table 3

15 PRO XXXXXXXXXX (Length = 10 amino acids)  
 Comparison Protein XXXXXYYYYYYZZYZ (Length = 15 amino acids)  
 % amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as  
 20 determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =  
 5 divided by 10 = 50%

Table 4

25 PRO-DNA NNNNNNNNNNNNNN (Length = 14 nucleotides)  
 Comparison DNA NNNNNNLLLLLLLLLL (Length = 16 nucleotides)  
 % nucleic acid sequence identity =

30 (the number of identically matching nucleotides between the two nucleic acid sequences as determined by  
 ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) =  
 6 divided by 14 = 42.9%

Table 5

35 PRO-DNA NNNNNNNNNNNN (Length = 12 nucleotides)  
 Comparison DNA NNNNLLLVV (Length = 9 nucleotides)  
 % nucleic acid sequence identity =

40

(the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) = 4 divided by 12 = 33.3%

## 5        II. Compositions and Methods of the Invention

### A.     Full-Length PRO Polypeptides

      The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO polypeptides. In particular, cDNAs encoding various PRO polypeptides have been identified and isolated, as disclosed in further detail in the Examples  
10 below. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of PRO, will be referred to as "PRO/number", regardless of their origin or mode of preparation.

      As disclosed in the Examples below, the sequence of various cDNA clones have been disclosed.

15 The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

### B.     PRO Polypeptide Variants

      In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated  
20 that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

      Variations in the native full-length sequence PRO or in various domains of the PRO described  
25 herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the PRO as compared with the native sequence PRO. Optionally, the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO.  
30 Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine,  
35 i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

      PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-  
40 terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native

protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO polypeptide.

PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments share at least one biological and/or immunological activity with the native PRO polypeptide disclosed herein.

In particular embodiments, conservative substitutions of interest are shown in Table 6 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 6, or as further described below in reference to amino acid classes, are introduced and the products screened.

Table 6

	Original Residue	Exemplary Substitutions	Preferred Substitutions
5	Ala (A)	val; leu; ile	val
	Arg (R)	lys; gln; asn	lys
	Asn (N)	gln; his; lys; arg	gln
	Asp (D)	glu	glu
10	Cys (C)	ser	ser
	Gln (Q)	asn	asn
	Glu (E)	asp	asp
	Gly (G)	pro; ala	ala
	His (H)	asn; gln; lys; arg	arg
15	Ile (I)	leu; val; met; ala; phe; norleucine	leu
	Leu (L)	norleucine; ile; val; met; ala; phe	ile
	Lys (K)	arg; gln; asn	arg
20	Met (M)	leu; phe; ile	leu
	Phe (F)	leu; val; ile; ala; tyr	leu
	Pro (P)	ala	ala
	Ser (S)	thr	thr
	Thr (T)	ser	ser
25	Trp (W)	tyr; phe	tyr
	Tyr (Y)	trp; phe; thr; ser	phe
	Val (V)	ile; leu; met; phe; ala; norleucine	leu

30 Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

- 35 (1) hydrophobic: norleucine, met, ala, val, leu, ile;  
 (2) neutral hydrophilic: cys, ser, thr;  
 (3) acidic: asp, glu;  
 (4) basic: asn, gln, his, lys, arg;  
 (5) residues that influence chain orientation: gly, pro; and  
 40 (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

45 The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., *Nucl. Acids Res.*, 13:4331 (1986); Zoller et al., *Nucl. Acids Res.*, 10:6487 (1987)], cassette mutagenesis [Wells et al., *Gene*, 34:315 (1985)], restriction selection mutagenesis [Wells et al., *Philos. Trans. R. Soc. London SerA*, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, Science, 244: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, The Proteins, (W.H. Freeman & Co., N.Y.); Chothia, J. Mol. Biol., 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

#### C. Modifications of PRO

Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO. Derivatization with bifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidyl)propionate, bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimide.

Other modifications include deamidation of glutamyl and asparaginy residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, ~~phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the  $\alpha$ -amino groups of~~ lysine, arginine, and histidine side chains [T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

5 Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved  
10 by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417;  
15 4,791,192 or 4,179,337.

The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising PRO fused to another, heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is  
20 generally placed at the amino- or carboxyl- terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine  
25 (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide  
30 [Martin et al., Science, 255:192-194 (1992)]; an alpha-tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule  
35 (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also US  
40 Patent No. 5,428,130 issued June 27, 1995.

#### D. Preparation of PRO

The description below relates primarily to production of PRO by culturing cells transformed or transfected with a vector containing PRO nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, CA (1969); Merrifield, J. Am. Chem. Soc., 85:2149-2154 (1963)]. *In vitro* protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the PRO may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length PRO.

##### 1. Isolation of DNA Encoding PRO

DNA encoding PRO may be obtained from a cDNA library prepared from tissue believed to possess the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PRO-encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as described in Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989). ~~An alternative means to isolate the gene encoding PRO is to use PCR methodology~~ [Sambrook et al., supra; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)].

The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like <sup>32</sup>P-labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., supra.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

## 2. Selection and Transformation of Host Cells

Host cells are transfected or transformed with expression or cloning vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in Mammalian Cell Biotechnology: a Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example,  $\text{CaCl}_2$ ,  $\text{CaPO}_4$ , liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., supra, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., Gene, 23:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, Virology, 52:456-457 (1978) can be employed. General aspects of mammalian cell host system transfections have been described in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., J. Bact., 130:946 (1977) and Hsiao et al., Proc. Natl. Acad. Sci. (USA), 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., Methods in Enzymology, 185:527-537 (1990) and Mansour et al., Nature, 336:348-352 (1988).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonA*; *E. coli* W3110 strain 9B4, which has the complete genotype *tonA ptr3*; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan'*; *E. coli* W3110 strain 37D6, which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kan'*; *E. coli* W3110 strain 40B4, which is strain



37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, Nature, 290: 140 [1981]; EP 139,383 published 2 May 1985); *Kluyveromyces* hosts (U.S. Patent No. 4,943,529; Fleer et al., Bio/Technology, 9:968-975 (1991)) such as, e.g., *K. lactis* (MW98-8C, CBS683, CBS4574; Louvencourt et al., J. Bacteriol., 154(2):737-742 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickerhamii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilae* (ATCC 36,906; Van den Berg et al., Bio/Technology, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus*; *yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna et al., J. Basic Microbiol., 28:265-278 [1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolyocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al., Gene, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4:475-479 [1985]). Methylophilic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, The Biochemistry of Methylophilic Yeasts, 269 (1982).

Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Sporoptera* Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen. Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

### 3. Selection and Use of a Replicable Vector

The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination

sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

The PRO may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the PRO-encoding DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g., the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces*  $\alpha$ -factor leaders, the latter described in U.S. Patent No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders.

Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 $\mu$  plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for *Bacilli*.

An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., *Proc. Natl. Acad. Sci. USA*, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., *Nature*, 282:39 (1979); Kingsman et al., *Gene*, 7:141 (1979); Tschemper et al., *Gene*, 10:157 (1980)]. The *trp1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-1 [Jones, *Genetics*, 85:12 (1977)].

Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoters suitable for use with prokaryotic hosts include the  $\beta$ -lactamase and lactose promoter systems [Chang et al., *Nature*, 275:615 (1978); Goeddel et al., *Nature*, 281:544 (1979)], alkaline phosphatase, a tryptophan (*trp*) promoter system [Goeddel, *Nucleic Acids Res.*, 8:4057 (1980); EP 36,776], and hybrid promoters such as the tac promoter [deBoer et al., *Proc. Natl. Acad. Sci. USA*, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding PRO.

Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., J. Biol. Chem., 255:2073 (1980)] or other glycolytic enzymes [Hess et al., J. Adv. Enzyme Reg., 7:149 (1968); Holland, Biochemistry, 17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 July 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin,  $\alpha$ -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the PRO coding sequence, but is preferably located at a site 5' from the promoter.

Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO.

Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO in recombinant vertebrate cell culture are described in Gething et al., Nature, 293:620-625 (1981); Mantei et al., Nature, 281:40-46 (1979); EP 117,060; and EP 117,058.

#### 4. Detecting Gene Amplification/Expression

Gene amplification and/or expression may be measured in a sample directly, for example, by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, Proc. Natl. Acad. Sci. USA, 77:5201-5205 (1980)], dot blotting (DNA analysis), or *in situ* hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be

employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to PRO DNA and encoding a specific antibody epitope.

#### 5. Purification of Polypeptide

Forms of PRO may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage. Cells employed in expression of PRO can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns to bind epitope-tagged forms of the PRO. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, Methods in Enzymology, 182 (1990); Scopes, Protein Purification: Principles and Practice, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for example, on the nature of the production process used and the particular PRO produced.

#### E. Tissue Distribution

The location of tissues expressing the PRO can be identified by determining mRNA expression in various human tissues. The location of such genes provides information about which tissues are most likely to be affected by the stimulating and inhibiting activities of the PRO polypeptides. The location of a gene in a specific tissue also provides sample tissue for the activity blocking assays discussed below.

As noted before, gene expression in various tissues may be measured by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA (Thomas, *Proc. Natl. Acad. Sci. USA*, 77:5201-5205 [1980]), dot blotting (DNA analysis), or *in situ* hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes.

Gene expression in various tissues, alternatively, may be measured by immunological methods, such as immunohistochemical staining of tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining

and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence of a PRO polypeptide or against a synthetic peptide based on the DNA sequences encoding the PRO polypeptide or against an exogenous sequence fused to a DNA encoding a PRO polypeptide and encoding a specific antibody epitope. General techniques for generating antibodies, and special protocols for Northern blotting and *in situ* hybridization are provided below.

#### F. Antibody Binding Studies

The activity of the PRO polypeptides can be further verified by antibody binding studies, in which the ability of anti-PRO antibodies to inhibit the effect of the PRO polypeptides, respectively, on tissue cells is tested. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies, the preparation of which will be described hereinbelow.

Antibody binding studies may be carried out in any known assay method, such as competitive binding assays, direct and indirect sandwich assays, and immunoprecipitation assays. Zola, *Monoclonal Antibodies: A Manual of Techniques*, pp.147-158 (CRC Press, Inc., 1987).

Competitive binding assays rely on the ability of a labeled standard to compete with the test sample analyte for binding with a limited amount of antibody. The amount of target protein in the test sample is inversely proportional to the amount of standard that becomes bound to the antibodies. To facilitate determining the amount of standard that becomes bound, the antibodies preferably are insolubilized before or after the competition, so that the standard and analyte that are bound to the antibodies may conveniently be separated from the standard and analyte which remain unbound.

Sandwich assays involve the use of two antibodies, each capable of binding to a different immunogenic portion, or epitope, of the protein to be detected. In a sandwich assay, the test sample analyte is bound by a first antibody which is immobilized on a solid support, and thereafter a second antibody binds to the analyte, thus forming an insoluble three-part complex. See, e.g., US Pat No. 4,376,110. The second antibody may itself be labeled with a detectable moiety (direct sandwich assays) or may be measured using an anti-immunoglobulin antibody that is labeled with a detectable moiety (indirect sandwich assay). For example, one type of sandwich assay is an ELISA assay, in which case the detectable moiety is an enzyme.

For immunohistochemistry, the tissue sample may be fresh or frozen or may be embedded in paraffin and fixed with a preservative such as formalin, for example.

#### G. Cell-Based Assays

Cell-based assays and animal models for immune related diseases such as psoriasis can be used to further understand the relationship between the genes and polypeptides identified herein and the development and pathogenesis psoriasis.

In a different approach, cells of a cell type known to be involved in psoriasis are transfected with the cDNAs described herein, and the ability of these cDNAs to stimulate or inhibit psoriasis is analyzed. Suitable cells can be transfected with the desired gene, and monitored for such functional activity. Such transfected cell lines can then be used to test the ability of poly- or monoclonal antibodies or antibody compositions to inhibit or stimulate psoriasis. Cells transfected with the coding sequences of the genes identified herein can further be used to identify drug candidates for the treatment of psoriasis.

In addition, primary cultures derived from transgenic animals (as described below) can be used in the cell-based assays herein, although stable cell lines are preferred. Techniques to derive continuous cell lines from transgenic animals are well known in the art (see, *e.g.*, Small *et al.*, *Mol. Cell. Biol.* **5**: 642-648 [1985]).

5           H.       Animal Models

The results of cell based *in vitro* assays can be further verified using *in vivo* animal models and assays for psoriasis. A variety of well known animal models can be used to further understand the role of the genes identified herein in the development and pathogenesis of psoriasis, and to test the efficacy of candidate therapeutic agents, including antibodies, and other antagonists of the native polypeptides, including small molecule antagonists. The *in vivo* nature of such models makes them predictive of responses in human patients. Animal models of immune related diseases include both non-recombinant and recombinant (transgenic) animals. Non-recombinant animal models include, for example, rodent, *e.g.*, murine models. Such models can be generated by introducing cells into syngeneic mice using standard techniques, *e.g.*, subcutaneous injection, tail vein injection, spleen implantation, intraperitoneal implantation, implantation under the renal capsule, *etc.*

Graft-versus-host disease occurs when immunocompetent cells are transplanted into immunosuppressed or tolerant patients. The donor cells recognize and respond to host antigens. The response can vary from life threatening severe inflammation to mild cases of diarrhea and weight loss. Graft-versus-host disease models provide a means of assessing T cell reactivity against MHC antigens and minor transplant antigens. A suitable procedure is described in detail in *Current Protocols in Immunology*, above, unit 4.3.

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An animal model for skin allograft rejection is a means of testing the ability of T cells to mediate *in vivo* tissue destruction and a measure of their role in transplant rejection. The most common and accepted models use murine tail-skin grafts. Repeated experiments have shown that skin allograft rejection is mediated by T cells, helper T cells and killer-effector T cells, and not antibodies. Auchincloss, H. Jr. and Sachs, D. H., *Fundamental Immunology*, 2nd ed., W. E. Paul ed., Raven Press, NY, 1989, 889-992. A suitable procedure is described in detail in *Current Protocols in Immunology*, above, unit 4.4. Other transplant rejection models which can be used to test the compounds of the invention are the allogeneic heart transplant models described by Tanabe, M. *et al*, *Transplantation* (1994) **58**:23 and Tinubu, S. A. *et al*, *J. Immunol.* (1994) 4330-4338.

Contact hypersensitivity is a simple delayed type hypersensitivity *in vivo* assay of cell mediated immune function. In this procedure, cutaneous exposure to exogenous haptens which gives rise to a delayed type hypersensitivity reaction which is measured and quantitated. Contact sensitivity involves an initial sensitizing phase followed by an elicitation phase. The elicitation phase occurs when the T lymphocytes encounter an antigen to which they have had previous contact. Swelling and inflammation occur, making this an excellent model of human allergic contact dermatitis. A suitable procedure is described in detail in *Current Protocols in Immunology*, Eds. J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach and W. Strober, John Wiley & Sons, Inc., 1994, unit 4.2. See also Grabbe, S. and Schwarz, T, *Immun. Today* **19** (1): 37-44 (1998).

Additionally, the compounds of the invention can be tested on animal models for psoriasis like diseases. Evidence suggests a T cell pathogenesis for psoriasis. The compounds of the invention can be tested in the scid/scid mouse model described by Schon, M. P. *et al*, *Nat. Med.* (1997) 3:183, in which the mice demonstrate histopathologic skin lesions resembling psoriasis. Another suitable model is the human skin/scid mouse chimera prepared as described by Nickoloff, B. J. *et al*, *Am. J. Path.* (1995) 146:580.

Recombinant (transgenic) animal models can be engineered by introducing the coding portion of the genes identified herein into the genome of animals of interest, using standard techniques for producing transgenic animals. Animals that can serve as a target for transgenic manipulation include, without limitation, mice, rats, rabbits, guinea pigs, sheep, goats, pigs, and non-human primates, *e.g.*, baboons, chimpanzees and monkeys. Techniques known in the art to introduce a transgene into such animals include pronucleic microinjection (Hoppe and Wanger, U.S. Patent No. 4,873,191); retrovirus-mediated gene transfer into germ lines (*e.g.*, Van der Putten *et al*, *Proc. Natl. Acad. Sci. USA* 82, 6148-615 [1985]); gene targeting in embryonic stem cells (Thompson *et al*, *Cell* 56, 313-321 [1989]); electroporation of embryos (Lo, *Mol. Cel. Biol.* 3, 1803-1814 [1983]); sperm-mediated gene transfer (Lavitrano *et al*, *Cell* 57, 717-73 [1989]). For review, see, for example, U.S. Patent No. 4,736,866.

For the purpose of the present invention, transgenic animals include those that carry the transgene only in part of their cells ("mosaic animals"). The transgene can be integrated either as a single transgene, or in concatamers, *e.g.*, head-to-head or head-to-tail tandems. Selective introduction of a transgene into a particular cell type is also possible by following, for example, the technique of Lasko *et al*, *Proc. Natl. Acad. Sci. USA* 89, 6232-636 (1992).

The expression of the transgene in transgenic animals can be monitored by standard techniques. For example, Southern blot analysis or PCR amplification can be used to verify the integration of the transgene. The level of mRNA expression can then be analyzed using techniques such as *in situ* hybridization, Northern blot analysis, PCR, or immunocytochemistry.

The animals may be further examined for signs of immune disease pathology, for example by histological examination to determine infiltration of immune cells into specific tissues. Blocking experiments can also be performed in which the transgenic animals are treated with the compounds of the invention to determine the extent of the T cell proliferation stimulation or inhibition of the compounds. In these experiments, blocking antibodies which bind to the PRO polypeptide, prepared as described above, are administered to the animal and the effect on immune function is determined.

Alternatively, "knock out" animals can be constructed which have a defective or altered gene encoding a polypeptide identified herein, as a result of homologous recombination between the endogenous gene encoding the polypeptide and altered genomic DNA encoding the same polypeptide introduced into an embryonic cell of the animal. For example, cDNA encoding a particular polypeptide can be used to clone genomic DNA encoding that polypeptide in accordance with established techniques. A portion of the genomic DNA encoding a particular polypeptide can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector [see *e.g.*, Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced DNA

has homologously recombined with the endogenous DNA are selected [see *e.g.*, Li *et al.*, *Cell*, **69**:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse or rat) to form aggregation chimeras [see *e.g.*, Bradley, in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can then be  
5 implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend against certain pathological conditions and for their development of pathological conditions due to  
10 absence of the polypeptide.

#### I. ImmunoAdjuvant Therapy

In one embodiment, the immunostimulating compounds of the invention can be used in immunoadjuvant therapy for the treatment of tumors (cancer). It is now well established that T cells recognize human tumor specific antigens. One group of tumor antigens, encoded by the MAGE, BAGE and  
15 GAGE families of genes, are silent in all adult normal tissues, but are expressed in significant amounts in tumors, such as melanomas, lung tumors, head and neck tumors, and bladder carcinomas. DeSmet, C. *et al.*, (1996) *Proc. Natl. Acad. Sci. USA*, **93**:7149. It has been shown that costimulation of T cells induces tumor regression and an antitumor response both *in vitro* and *in vivo*. Melero, I. *et al.*, *Nature Medicine* (1997) **3**:682; Kwon, E. D. *et al.*, *Proc. Natl. Acad. Sci. USA* (1997) **94**: 8099; Lynch, D. H. *et al.*, *Nature Medicine*  
20 (1997) **3**:625; Finn, O. J. and Lotze, M. T., *J. Immunol.* (1998) **21**:114. The stimulatory compounds of the invention can be administered as adjuvants, alone or together with a growth regulating agent, cytotoxic agent or chemotherapeutic agent, to stimulate T-cell proliferation/activation and an antitumor response to tumor antigens. The growth regulating, cytotoxic, or chemotherapeutic agent may be administered in conventional amounts using known administration regimes. Immunostimulating activity by the compounds of the  
25 invention allows reduced amounts of the growth regulating, cytotoxic, or chemotherapeutic agents thereby potentially lowering the toxicity to the patient.

#### I. Screening Assays for Drug Candidates

Screening assays for drug candidates are designed to identify compounds that bind to or complex with the polypeptides encoded by the genes identified herein or a biologically active fragment thereof, or  
30 otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds, including peptides, preferably soluble peptides, (poly)peptide-immunoglobulin fusions, and, in particular, antibodies including, without limitation, poly- and  
35 monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art. All assays are common in that they call for contacting the drug candidate with a polypeptide encoded by a  
40 nucleic acid identified herein under conditions and for a time sufficient to allow these two components to



interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, *e.g.*, on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the polypeptide and drying. Alternatively, an immobilized antibody, *e.g.*, a monoclonal antibody, specific for the polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, *e.g.*, the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, *e.g.*, by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labelled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular protein encoded by a gene identified herein, its interaction with that protein can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers [Fields and Song, *Nature (London)* 340, 245-246 (1989); Chien *et al.*, *Proc. Natl. Acad. Sci. USA* 88, 9578-9582 (1991)] as disclosed by Chevray and Nathans, *Proc. Natl. Acad. Sci. USA* 89, 5789-5793 (1991). ~~Many transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, while the other one functioning as the transcription activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-*lacZ* reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for  $\beta$ -galactosidase. A complete kit (MATCHMAKER<sup>TM</sup>) for identifying protein-protein interactions between two specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.~~

In order to find compounds that interfere with the interaction of a gene identified herein and other intra- or extracellular components can be tested, a reaction mixture is usually prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a test compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described above.

The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

K. Compositions and Methods for the Treatment of Psoriasis

The compositions useful in the treatment of psoriasis include, without limitation, proteins, antibodies, small organic molecules, peptides, phosphopeptides, antisense and ribozyme molecules, triple helix molecules, *etc.* that inhibit immune function, for example, T cell proliferation/activation, lymphokine release, or immune cell infiltration.

For example, antisense RNA and RNA molecules act to directly block the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation initiation site, *e.g.*, between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, *e.g.*, Rossi, *Current Biology* 4, 469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

Nucleic acid molecules in triple helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple helix formation via Hoogsteen base pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, *e.g.*, PCT publication No. WO 97/33551, *supra*.

These molecules can be identified by any or any combination of the screening assays discussed above and/or by any other screening techniques well known for those skilled in the art.

L. Anti-PRO Antibodies

The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

1. Polyclonal Antibodies

The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

## 2. Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980).

After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, *supra*]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison et al., *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

*In vitro* methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

### 3. Human and Humanized Antibodies

The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')<sub>2</sub> or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985) and Boerner et al., *J. Immunol.*, 147(1):86-95 (1991)). Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., *Bio/Technology* 10, 779-783 (1992); Lonberg et al., *Nature* 368 856-859 (1994); Morrison, *Nature* 368, 812-13 (1994); Fishwild et al., *Nature Biotechnology* 14, 845-51 (1996); Neuberger, *Nature Biotechnology* 14, 826 (1996); Lonberg and Huszar, *Intern. Rev. Immunol.* 13 65-93 (1995).

The antibodies may also be affinity matured using known selection and/or mutagenesis methods as described above. Preferred affinity matured antibodies have an affinity which is five times, more preferably 10 times, even more preferably 20 or 30 times greater than the starting antibody (generally murine, humanized or human) from which the matured antibody is prepared.

#### 4. Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, *Nature*, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by

affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker et al., EMBO J., 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an

5 immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions.

It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for  
10 example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first  
15 antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')<sub>2</sub> bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been  
20 described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan *et al.*, Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')<sub>2</sub> fragments. These fragments are reduced in the presence of the  
25 dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific  
30 antibodies. Shalaby *et al.*, J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')<sub>2</sub> molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well  
35 as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny *et al.*, J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion.

40 The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form

the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al.*, Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V<sub>H</sub>) connected to a light-chain variable domain (V<sub>L</sub>) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V<sub>H</sub> and V<sub>L</sub> domains of one fragment are forced to pair with the complementary V<sub>L</sub> and V<sub>H</sub> domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber *et al.*, J. Immunol. 152:5368 (1994). Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt *et al.*, J. Immunol. 147:60 (1991).

Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

#### 5. Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. ~~Heteroconjugate antibodies are composed of two covalently joined antibodies.~~ Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro* using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

#### 6. Effector Function Engineering

It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, *e.g.*, the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron *et al.*, J. Exp. Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff *et al.* Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson *et al.*, Anti-Cancer Drug Design, 3: 219-230 (1989).

## 7. Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolacca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include  $^{212}\text{Bi}$ ,  $^{131}\text{I}$ ,  $^{131}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{186}\text{Re}$ .

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta *et al.*, Science, **238**: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is conjugated to a cytotoxic agent (e.g., a radionucleotide).

## 8. Immunoliposomes

The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, **82**: 3688 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA, **77**: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No. 5,013,556.

Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin *et al.*, J. Biol. Chem., **257**: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon *et al.*, J. National Cancer Inst., **81**(19): 1484 (1989).

## M. Pharmaceutical Compositions



The active PRO molecules of the invention (e.g., PRO polypeptides, anti-PRO antibodies, and/or variants of each) as well as other molecules identified by the screening assays disclosed above, can be administered for the treatment of psoriasis, in the form of pharmaceutical compositions.

Therapeutic formulations of the active PRO molecule, preferably a polypeptide or antibody of the invention, are prepared for storage by mixing the active molecule having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers (*Remington's Pharmaceutical Sciences* 16th edition, Osol, A. Ed. [1980]), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEEN<sup>TM</sup>, PLURONICS<sup>TM</sup> or polyethylene glycol (PEG).

Compounds identified by the screening assays disclosed herein can be formulated in an analogous manner, using standard techniques well known in the art.

~~Lipofections or liposomes can also be used to deliver the PRO molecule into cells. Where antibody~~  
fragments are used, the smallest inhibitory fragment which specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable region sequences of an antibody, peptide molecules can be designed which retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology (see, e.g., Marasco *et al.*, *Proc. Natl. Acad. Sci. USA* 90, 7889-7893 [1993]).

The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise a cytotoxic agent, cytokine or growth inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active PRO molecules may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in *Remington's Pharmaceutical Sciences* 16th edition, Osol, A. Ed. (1980).

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

Sustained-release preparations of the PRO molecules may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, *e.g.*, films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and  $\gamma$ -ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT<sup>TM</sup> (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

#### N. Methods of Treatment

It is contemplated that the polypeptides, antibodies and other active compounds of the present invention may be used to treat psoriasis and related conditions, such as T cell mediated diseases, including those characterized by infiltration of inflammatory cells into a tissue.

Spondyloarthropathies are a group of disorders with some common clinical features and the common association with the expression of HLA-B27 gene product. The disorders include: ankylosing spondylitis, Reiter's syndrome (reactive arthritis), arthritis associated with inflammatory bowel disease, spondylitis associated with psoriasis, juvenile onset spondyloarthropathy and undifferentiated spondyloarthropathy. Distinguishing features include sacroileitis with or without spondylitis; inflammatory asymmetric arthritis; association with HLA-B27 (a serologically defined allele of the HLA-B locus of class I MHC); ocular inflammation, and absence of autoantibodies associated with other rheumatoid disease. The cell most implicated as key to induction of the disease is the CD8+ T lymphocyte, a cell which targets antigen presented by class I MHC molecules. CD8+ T cells may react against the class I MHC allele HLA-B27 as if it were a foreign peptide expressed by MHC class I molecules. It has been hypothesized that an epitope of HLA-B27 may mimic a bacterial or other microbial antigenic epitope and thus induce a CD8+ T cells response.

Systemic sclerosis (scleroderma) has an unknown etiology. A hallmark of the disease is induration of the skin; likely this is induced by an active inflammatory process. Scleroderma can be localized or systemic; vascular lesions are common and endothelial cell injury in the microvasculature is an early and important event in the development of systemic sclerosis; the vascular injury may be immune mediated. An immunologic basis is implied by the presence of mononuclear cell infiltrates in the cutaneous lesions and the presence of anti-nuclear antibodies in many patients. ICAM-1 is often upregulated on the cell surface of fibroblasts in skin lesions suggesting that T cell interaction with these cells may have a role in the pathogenesis of the disease. Other organs involved include: the gastrointestinal tract; smooth muscle

atrophy and fibrosis resulting in abnormal peristalsis/motility; kidney: concentric subendothelial intimal proliferation affecting small arcuate and interlobular arteries with resultant reduced renal cortical blood flow, results in proteinuria, azotemia and hypertension; skeletal muscle: atrophy, interstitial fibrosis; inflammation; lung: interstitial pneumonitis and interstitial fibrosis; and heart: contraction band necrosis, scarring/fibrosis.

Autoimmune or Immune-mediated Skin Disease including Bullous Skin Diseases, Erythema Multiforme, and Contact Dermatitis are mediated by auto-antibodies, the genesis of which is T lymphocyte-dependent.

Psoriasis is proposed to be a T lymphocyte-mediated inflammatory disease. Lesions contain infiltrates of T lymphocytes, macrophages and antigen processing cells, and some neutrophils.

Transplantation associated diseases, including Graft rejection and Graft-Versus-Host-Disease (GVHD) are T lymphocyte-dependent; inhibition of T lymphocyte function is ameliorative.

The compounds of the present invention, e.g., polypeptides or antibodies, are administered to a mammal, preferably a human, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intracerebrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation (intranasal, intrapulmonary) routes. Intravenous or inhaled administration of polypeptides and antibodies is preferred.

In immunoadjuvant therapy, other therapeutic regimens, such administration of an anti-cancer agent, may be combined with the administration of the proteins, antibodies or compounds of the instant invention. For example, the patient to be treated with a the immunoadjuvant of the invention may also receive an anti-cancer agent (chemotherapeutic agent) or radiation therapy. Preparation and dosing schedules for such chemotherapeutic agents may be used according to manufacturers' instructions or as determined empirically by the skilled practitioner. Preparation and dosing schedules for such chemotherapy are also described in *Chemotherapy Service* Ed., M.C. Perry, Williams & Wilkins, Baltimore, MD (1992). The chemotherapeutic agent may precede, or follow administration of the immunoadjuvant or may be given simultaneously therewith. Additionally, an anti-estrogen compound such as tamoxifen or an anti-progesterone such as onapristone (see, EP 616812) may be given in dosages known for such molecules.

It may be desirable to also administer antibodies against other immune disease associated or tumor associated antigens, such as antibodies which bind to CD20, CD11a, CD18, ErbB2, EGFR, ErbB3, ErbB4, or vascular endothelial factor (VEGF). Alternatively, or in addition, two or more antibodies binding the same or two or more different antigens disclosed herein may be coadministered to the patient. Sometimes, it may be beneficial to also administer one or more cytokines to the patient. In one embodiment, the PRO polypeptides are coadministered with a growth inhibitory agent. For example, the growth inhibitory agent may be administered first, followed by a PRO polypeptide. However, simultaneous administration or administration first is also contemplated. Suitable dosages for the growth inhibitory agent are those presently used and may be lowered due to the combined action (synergy) of the growth inhibitory agent and the PRO polypeptide.

For the treatment or reduction in the severity of immune related disease, the appropriate dosage of an a compound of the invention will depend on the type of disease to be treated, as defined above, the severity and course of the disease, whether the agent is administered for preventive or therapeutic purposes,

previous therapy, the patient's clinical history and response to the compound, and the discretion of the attending physician. The compound is suitably administered to the patient at one time or over a series of treatments.

For example, depending on the type and severity of the disease, about 1 µg/kg to 15 mg/kg (*e.g.*, 0.1-20 mg/kg) of polypeptide or antibody is an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. A typical daily dosage might range from about 1 µg/kg to 100 mg/kg or more, depending on the factors mentioned above. For repeated administrations over several days or longer, depending on the condition, the treatment is sustained until a desired suppression of disease symptoms occurs. However, other dosage regimens may be useful. The progress of this therapy is easily monitored by conventional techniques and assays.

O. Articles of Manufacture

In another embodiment of the invention, an article of manufacture containing materials (*e.g.*, comprising a PRO molecule) useful for the diagnosis or treatment of the disorders described above is provided. The article of manufacture comprises a container and an instruction. Suitable containers include, for example, bottles, vials, syringes, and test tubes. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition which is effective for diagnosing or treating the condition and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The active agent in the composition is usually a polypeptide or an antibody of the invention. An instruction or label on, or associated with, the container indicates that the composition is used for diagnosing or treating the condition of choice. The article of manufacture may further comprise a second container comprising a pharmaceutically-acceptable buffer, such as phosphate-buffered saline, Ringer's solution and dextrose solution. It may further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, syringes, and package inserts with instructions for use.

P. Diagnosis and Prognosis of Immune Related Disease

Cell surface proteins, such as proteins which are overexpressed in psoriasis, are excellent targets for drug candidates or disease treatment. The same proteins along with secreted proteins encoded by the genes amplified in psoriasis find additional use in the diagnosis and prognosis of this disease. For example, antibodies directed against the protein products of genes amplified psoriasis, can be used as diagnostics or prognostics.

For example, antibodies, including antibody fragments, can be used to qualitatively or quantitatively detect the expression of proteins encoded by amplified or overexpressed genes ("marker gene products"). The antibody preferably is equipped with a detectable, *e.g.*, fluorescent label, and binding can be monitored by light microscopy, flow cytometry, fluorimetry, or other techniques known in the art. These techniques are particularly suitable, if the overexpressed gene encodes a cell surface protein. Such binding assays are performed essentially as described above.

*In situ* detection of antibody binding to the marker gene products can be performed, for example, by immunofluorescence or immunoelectron microscopy. For this purpose, a histological specimen is removed from the patient, and a labeled antibody is applied to it, preferably by overlaying the antibody on a biological sample. This procedure also allows for determining the distribution of the marker gene product in the tissue

examined. It will be apparent for those skilled in the art that a wide variety of histological methods are readily available for *in situ* detection.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

- 5 All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

#### EXAMPLES

- 10 Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, VA.

##### EXAMPLE 1: Microarray analysis of PRO in Psoriasis

- 15 Skin biopsies from psoriatic patients and from healthy donors ( henceforth, "normal skin") were obtained. For each psoriatic patient, skin samples were taken from lesional and non-lesional sites, in order to identify disease specific genes which are differentially expressed in psoriatic tissue. All of the psoriatic skin samples were analyzed for Keratin16 staining via immunohistochemistry and epidermal thickness. All samples were stored at -70 °C until ready for RNA isolation. The skin biopsies were homogenized in 600µl of RLT buffer (+ BME) and RNA was isolated using Qiagen™ Rneasy Mini columns ( Qiagen ) with on-
- 20 column DNase treatment following the manufacturer's guidelines. Following RNA isolation, RNA was quantitated using RiboGreen™ (Molecular Probes ) following the manufacturer's guidelines and checked on agarose gels for integrity. The RNA yields ranged from 19 to 54 µg for psoriatic lesional skin, 7.7 to 24 µg for non-lesional matched control skin and 5.4 to 10µg for normal skin. 4µg of RNA was labeled for microarray analysis and samples were run on proprietary Genentech microarray and Affymetrics
- 25 microarrays. Genes were compared whose expression was upregulated or downregulated in psoriatic skin vs non-lesional skin, thus comparing expression profiles of non-lesional skin and psoriatic skin from the same patient, and also comparing against normal skin biopsies of normal healthy donors as a further control. The conclusion of this experiment is that the nucleic acids and encoded proteins of Figures 1-2484 are differentially expressed in psoriasis lesional skin in comparison to matched non-lesional skin from psoriasis
- 30 patients and normal skin taken from subjects without psoriasis. The nucleic acids and encoded proteins of Figure 13, Figure 336, Figure 393, Figure 477, Figure 513, Figure 593, Figure 853, Figure 1004, Figure 1283, Figure 1730, Figure 1861 and Figure 2227 are significantly overexpressed in psoriasis lesional skin compared to matched non-lesional skin from psoriasis patients and normal skin taken from subjects without psoriasis.

##### 35 EXAMPLE 2: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

- 40 DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

#### EXAMPLE 3: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. ~~Transformants are identified by their ability to grow on LB plates and antibiotic~~ resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium

citrate•2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO<sub>4</sub>) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

5 *E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of  
10 metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by  
15 its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is  
20 quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. ~~The refolded protein is chromatographed on a Poros R1/H reversed phase~~  
column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions  
25 containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

30 Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### 35 EXAMPLE 4: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

40 The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion

of the PRO DNA using ligation methods such as described in Sambrook et al., *supra*. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 µg pRK5-PRO DNA is mixed with about 1 µg DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500 µl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl<sub>2</sub>. To this mixture is added, dropwise, 500 µl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO<sub>4</sub>, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 µCi/ml <sup>35</sup>S-cysteine and 200 µCi/ml <sup>35</sup>S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompayrac et al., *Proc. Natl. Acad. Sci.*, 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 µg pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 µg/ml bovine insulin and 0.1 µg/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO<sub>4</sub> or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as <sup>35</sup>S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 promoter/enhancer containing vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 promoter/enhancer containing vector. Labeling may be performed, as described above, to verify expression.



The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by  $\text{Ni}^{2+}$ -chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

5 Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

10 Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR  
15 expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Quiagen), Dosper® or Fugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately  $3 \times 10^7$  cells are frozen in an ampule for further growth and production as described below.

20 The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mL of media and centrifuged at 1000 rpm for 5 minutes. ~~The supernatant is aspirated and the cells are resuspended in 10 mL of selective~~  
media (0.2  $\mu\text{m}$  filtered PS20 with 5% 0.2  $\mu\text{m}$  diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a  
25 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with  $3 \times 10^5$  cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at  $1.2 \times 10^6$  cells/mL. On day 0, pH is determined. On  
30 day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22  $\mu\text{m}$  filter.  
35 The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column  
40 is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing

0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 µl of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 5: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 6: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction

enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni<sup>2+</sup>-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 µm filter. A Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A<sub>280</sub> with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A<sub>280</sub> baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni<sup>2+</sup>-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His<sub>10</sub>-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 7: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, supra. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions  
5 generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the  
10 art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion  
15 chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

#### EXAMPLE 8: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the  
20 art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with  
25 ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed  
30 according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide  
35 containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt

antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

#### EXAMPLE 9: Drug Screening

5 This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment.

10 Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

15 Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays,  
20 the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a ~~measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO~~  
polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having  
25 suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the  
30 aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of  
35 any peptide which shares one or more antigenic determinants with PRO polypeptide.

#### EXAMPLE 10: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists,  
40 antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or

stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (c.f., Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of a PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

What is claimed:

1. Isolated nucleic acid comprising at least 80% nucleic acid sequence identity to a  
 5 nucleotide sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:3), Figure 5 (SEQ ID NO:5),  
 Figure 7 (SEQ ID NO:7), Figure 9A-B (SEQ ID NO:9), Figure 11 (SEQ ID NO:11), Figure 13 (SEQ ID  
 NO:13), Figure 15A-B (SEQ ID NO:15), Figure 17 (SEQ ID NO:17), Figure 19 (SEQ ID NO:19), Figure 21  
 (SEQ ID NO:21), Figure 23A-B (SEQ ID NO:23), Figure 25 (SEQ ID NO:25), Figure 27A-C (SEQ ID  
 NO:27), Figure 29 (SEQ ID NO:29), Figure 31 (SEQ ID NO:31), Figure 33A-B (SEQ ID NO:33), Figure 35  
 10 (SEQ ID NO:35), Figure 37 (SEQ ID NO:37), Figure 39 (SEQ ID NO:39), Figure 41 (SEQ ID NO:41),  
 Figure 42 (SEQ ID NO:42), Figure 45 (SEQ ID NO:45), Figure 47 (SEQ ID NO:47), Figure 49 (SEQ ID  
 NO:49), Figure 51 (SEQ ID NO:51), Figure 53 (SEQ ID NO:53), Figure 55A-B (SEQ ID NO:55), Figure 57  
 (SEQ ID NO:57), Figure 59 (SEQ ID NO:59), Figure 61 (SEQ ID NO:61), Figure 63A-B (SEQ ID NO:63),  
 Figure 65 (SEQ ID NO:65), Figure 67A-B (SEQ ID NO:67), Figure 69 (SEQ ID NO:69), Figure 71A-B  
 15 (SEQ ID NO:71), Figure 73 (SEQ ID NO:73), Figure 75 (SEQ ID NO:75), Figure 77 (SEQ ID NO:77),  
 Figure 79 (SEQ ID NO:79), Figure 81 (SEQ ID NO:81), Figure 83 (SEQ ID NO:83), Figure 85 (SEQ ID  
 NO:85), Figure 87 (SEQ ID NO:87), Figure 89 (SEQ ID NO:89), Figure 91 (SEQ ID NO:91), Figure 93A-B  
 (SEQ ID NO:93), Figure 95A-B (SEQ ID NO:95), Figure 97 (SEQ ID NO:97), Figure 99 (SEQ ID NO:99),  
 Figure 101 (SEQ ID NO:101), Figure 103 (SEQ ID NO:103), Figure 105 (SEQ ID NO:105), Figure 107  
 20 (SEQ ID NO:107), Figure 109 (SEQ ID NO:109), Figure 111A-B (SEQ ID NO:111), Figure 113 (SEQ ID  
 NO:113), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118),  
~~Figure 120A-B (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124A-B (SEQ ID NO:124), Figure~~  
 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID  
 NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138A-B (SEQ ID NO:138),  
 25 Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146  
 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152A-B (SEQ ID  
 NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158A-B (SEQ ID NO:158),  
 Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164A-B (SEQ ID NO:164), Figure 166  
 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID  
 30 NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178),  
 Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184A-B (SEQ ID NO:184), Figure 186  
 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192A-B (SEQ ID  
 NO:192), Figure 193 (SEQ ID NO:193), Figure 195A-B (SEQ ID NO:195), Figure 197 (SEQ ID NO:197),  
 Figure 199 (SEQ ID NO:199), Figure 201A-B (SEQ ID NO:201), Figure 203A-B (SEQ ID NO:203), Figure  
 35 205A-B (SEQ ID NO:205), Figure 207A-B (SEQ ID NO:207), Figure 209 (SEQ ID NO:209), Figure 211  
 (SEQ ID NO:211), Figure 213A-B (SEQ ID NO:213), Figure 215 (SEQ ID NO:215), Figure 217 (SEQ ID  
 NO:217), Figure 219 (SEQ ID NO:219), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222),  
 Figure 224A-B (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230  
 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID  
 40 NO:236), Figure 238 (SEQ ID NO:238), Figure 240A-D (SEQ ID NO:240), Figure 242 (SEQ ID NO:242),

1803/2777  
**FIGURE 1607**

SLHLSERADWQYSQRELDAVEVFFSRTARDNRLGCMFVRCAPSSRYTLLFSHGNAVDLGQMCSFYIGLGSRINCN  
IFSVDYSGYGVSSGKPSEKNLYADIDAAWQALRTRYGVSPENIILYGQSIGTVPTVDLASRYECAAVILHSPLMS  
GLRVAFPDTRKTYCFDAFPSIDKISKVISPVLVIHGTEDEVIDFSHGLAMYERCPRAVEPLWVEGAGHNDIELYA  
QYLERLKQFISHELPNS



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